

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

4/4

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61J 3/07	A1	(11) International Publication Number: WO 92/21311 (43) International Publication Date: 10 December 1992 (10.12.92)
(21) International Application Number: PCT/US92/04457		(74) Agents: SUNSTEIN, Bruce, D. et al.; Bromberg & Sunstein, 10 West Street, Boston, MA 02111 (US).
(22) International Filing Date: 29 May 1992 (29.05.92)		(81) Designated States: AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE (European patent), DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL (European patent), NO, PL, RO, RU, SD, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent).
(30) Priority data: 708,023 31 May 1991 (31.05.91) US		
(71) Applicant: GS TECHNOLOGIES, INC. [US/US]; 311 West Broadway Avenue, Fairfield, IA 52556 (US).		
(72) Inventors: GROSSWALD, Ralph, R. ; 311 West Broadway Avenue, Fairfield, IA 52556 (US). ANDERSON, Jeffery, B. ; 1525 South 400 East, #35, Provo, UT 84663 (US). ANDREW, Clair, S. ; 129 Wymouth Terrace, #3, Provo, UT 84604 (US).		
<p>PP03-0113 00 WO-CG 03.10.14</p> <p>SEARCH REPORT</p>		<p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
(54) Title: METHOD AND APPARATUS FOR THE MANUFACTURE OF PHARMACEUTICAL CELLULOSE CAPSULES		
(57) Abstract		
<p>A method and apparatus for manufacturing pharmaceutical capsules use an aqueous solution of a thermogelling cellulose ether composition and use capsule body pins and capsule cap pins as molds. The method involves heating the pins, dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins, removing the pins and drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps. Pins are heated pre-dip and post-dip to facilitate gelating. Counterflow air is applied to provide drying from the inside. Capsule parts are removed by gripping. Capsule parts may have a thick wall and a stiffening ring.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FI	Finland	ML	Mali
AU	Australia	FR	France	MN	Mongolia
BB	Barbados	GA	Gabon	MR	Mauritania
BE	Belgium	GB	United Kingdom	MW	Malawi
BF	Burkina Faso	CN	Guinea	NL	Netherlands
BG	Bulgaria	GR	Greece	NO	Norway
BJ	Benin	HU	Hungary	PL	Poland
BR	Brazil	IE	Ireland	RO	Romania
CA	Canada	IT	Italy	RU	Russian Federation
CF	Central African Republic	JP	Japan	SD	Sudan
CG	Congo	KP	Democratic People's Republic of Korea	SE	Sweden
CH	Switzerland	KR	Republic of Korea	SN	Senegal
CI	Côte d'Ivoire	LI	Liechtenstein	SU	Soviet Union
CM	Cameroon	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TC	Togo
DE	Germany	MC	Monaco	US	United States of America
DK	Denmark	MG	Madagascar		
ES	Spain				

-1-

METHOD AND APPARATUS FOR THE
MANUFACTURE OF PHARMACEUTICAL CELLULOSE CAPSULES

5

Technical Field of the Invention

The invention relates generally to methods and apparatus used in the manufacture of pharmaceutical capsules.

10

Background of the Invention

Pharmaceutical capsules presently in general use are made of gelatin and the techniques for the manufacture of gelatin capsules are well developed. Compositions for cellulose capsules are also well known, but the first 15 cellulose composition that was used commercially to manufacture cellulose capsules did not reliably break down in the user's digestive system. When this fact was discovered, the commercial manufacture of cellulose capsules was discontinued. An improved cellulose composition was 20 later patented by Sarkar and several patents disclose methods for manufacturing cellulose capsules from the improved cellulose composition. However, in the fifteen years since the Sarkar patent issued, and in spite of many attempts, none have succeeded in manufacturing cellulose 25 capsules in quantity, using the improved composition, with sufficient uniformity to be suitable for filling in modern high-speed filling machines. Until the present invention was made, cellulose capsules manufactured in quantity from the improved composition suffered imperfections such as 30 wrinkles, starred ends and corrugations. These imperfections result in capsules either breaking, failing to separate, or jamming in the high-speed filling machine.

Prior Art Gelatin Capsules

Prior art gelatin capsules, as shown in Figs. 1A, 1B 35 and 1C, are made in a range of sizes including sizes listed in the first column of each of Tables 1 and 2. These tables are copied from the February, 1987 Specification Sheet of the CAPSUGEL Division of Warner-Lambert Company for its PRE-FIT™, SNAP-FIT™ and CONI-SNAP™ series of hard gelatin

- 2 -

capsules. Table 1 shows the external diameter, obtained by optical measurements, of a body and a cap of each size of CAPSUGEL capsule. (Diameter is difficult to measure precisely because of the slightly tapered shape and the flexibility of the gelatin capsule parts.) Table 2 shows the target wall thickness of a body and a cap of each type and size of CAPSUGEL capsule. Table 3, copied from the Scherer LOX-IT™ specification sheet, gives the external diameter of the Scherer LOX-IT™ capsule caps and bodies in a range of sizes.

15

20

25

PRE-FIT™ SNAP-FIT™ or CONI-SNAP™					
sizes	Body		Cap		
	Inches	mm	Inches	mm	
000	0.373	9.60	0.394	10.00	
00	0.324	8.23	0.339	8.60	
0 el	0.291	7.38	0.300	7.70	
0	0.291	7.38	0.303	7.70	
1	0.263	6.68	0.275	6.98	
2	0.241	6.13	0.252	6.41	
3	0.221	5.61	0.231	5.88	
4 el	0.201	5.11	0.212	5.38	
4	0.201	5.11	0.212	5.38	
5	0.185	4.70	0.193	4.89	

Tolerance: ±0.001 (±0.03 mm)

TABLE 1 - CAPSUGEL CAPSULE PART, EXTERNAL DIAMETER

- 3 -

		PRE-FIT™				SNAP-FIT™ or CONI-SNAP™			
		Body		Cap		Body		Cap	
Size		Inches	mm	Inches	mm	Inches	mm	Inches	mm
5	000	0.0042 ±0.0009	0.107 ±0.023	0.0044 ±0.0012	0.112 ±0.030	—	—	—	—
	00	0.0041 ±0.0009	0.104 ±0.023	0.0042 ±0.0012	0.109 ±0.030	0.0042 ±0.0009	0.107 ±0.023	0.0043 ±0.0012	0.109 ±0.030
	0 el	—	—	—	—	0.0041 ±0.0008	0.104 ±0.020	0.0042 ±0.0010	0.107 ±0.025
	0	0.0040 ±0.0008	0.102 ±0.020	0.0042 ±0.0010	0.107 ±0.025	0.0041 ±0.0008	0.104 ±0.020	0.0042 ±0.0010	0.107 ±0.025
	1	0.0039 ±0.0008	0.099 ±0.020	0.0041 ±0.0010	0.104 ±0.025	0.0040 ±0.0008	0.102 ±0.020	0.0041 ±0.0010	0.104 ±0.025
10	2	0.0038 ±0.0008	0.096 ±0.020	0.0040 ±0.0010	0.102 ±0.025	0.0039 ±0.0008	0.099 ±0.020	0.0040 ±0.0010	0.102 ±0.025
	3*	0.0034 ±0.0008	0.086 ±0.020	0.0036 ±0.0010	0.092 ±0.025	0.0035 ±0.0008	0.089 ±0.020	0.0036 ±0.0010	0.092 ±0.025
	4 el	—	—	—	—	0.0037 ±0.0008	0.094 ±0.020	0.0038 ±0.0010	0.096 ±0.025
	4	0.0034 ±0.0008	0.086 ±0.020	0.0036 ±0.0010	0.089 ±0.025	0.0034 ±0.0008	0.086 ±0.020	0.0035 ±0.0010	0.091 ±0.025
	5	0.0034 ±0.0008	0.086 ±0.020	0.0036 ±0.0010	0.092 ±0.025	—	—	—	—

3* SNAP-FIT™ Body Target — 0.0034 ± 0.0008

15

TABLE 2 - CAPSULE CAPSULE PART, SINGLE WALL THICKNESS

20

25

Size	0	1	2	3	4
CAP DIAMETER* (±0.003)	0.301"	0.272"	0.250"	0.230"	0.210"
BODY DIAMETER* (±0.003)	0.289"	0.262"	0.240"	0.220"	0.200"

*DETERMINED AT CUT EDGE

TABLE 3 - SCHERER LOX-IT™ CAPSULE PART DIAMETER

- 4 -

U.S. Patent No. 3,399,803 to Oglevee et al. is directed to a hard-shell self-locking pharmaceutical capsule having a cap part and a body part, the parts adapted for machine filling. Oglevee discloses mold pins having a uniform taper or candle-shape such as to avoid suction when the part is removed from the pin and to provide a wedging fit between the capsule cap and the capsule body. Oglevee also discloses the shaping of the cap and body to provide a semi-locked position and a locked position. A single groove in the cap and a matching single groove in the body provide a mechanical lock.

U.S. Patent Nos. 3,508,678 and 3,664,495 both to Graham et al. disclose a capsule cap having an indent, in addition to a locking groove, which defines a prelock position by providing either an elastic friction fit with the capsule body (3,664,495) or a mechanical lock between the indent of the cap and the groove in the body (3,508,678).

U.S. Patent No. 4,247,006 to Bodenmann et al. discloses a capsule body having a reduced diameter in the area of its open end, and further the capsule cap and the capsule body each having an indentation to provide for a positive engagement of the body and the cap.

Prior Art Process for Gelatin Capsules

U.S. Patent No. 1,787,777 to Colton describes the "Colton" machine used in the manufacture of gelatin capsules. Key elements in the prior art manufacture of gelatin capsules are illustrated in Figs. 1-7. Fig. 1A shows the parts of a capsule having a body 1 and a cap 2. The parts are shown in Fig. 1B in a prelock position 3 held in position by prelock dimples 4. The parts are also shown in Fig. 1C in a filled position 5 held in position by locking rings 6. Fig. 2 shows elements of the traditional "Colton" capsule manufacturing machine. The elements are a greaser section 21, a dipper section 22, spinners 23, upper drying kiln 24, lower drying kiln 26, table section 27 and automatics 28. A pinbar, having thirty pins 31 mounted to a bar 32, is shown in Fig. 3. Fig. 4 shows gel 41 formed

- 5 -

around a pin 31 to a dip line 42. Also shown is the trim line (cut-point) 43 and the area 44 on the pin above the dip line. Fig. 5 shows a prior art stripper 51 about to push a capsule part 53 off a pin from the area 44 above the dip line with pushing face 52. A side view of a prior art stripper having a pivot 61 and a spring 62 is shown in Fig. 6. Fig. 7 shows a knife 71 trimming a capsule part to remove the rough edge 72 and create a clean edge 73.

U.S. Patent Nos. 1,978,829 (to Wilkie), 3,632,700 (to 10 Oglevee), 3,794,453 (to Padilla et al.), 4,705,658 (to Lukas) and 4,997,359 (to Lebrun) are all directed to processes for manufacturing gelatin capsules. The Wilkie patent discloses an apparatus for drying capsules by directing a stream of air at the part of the capsule that 15 contains the most moisture. A fine stream of air passing through a hole in a plate is directed to the closed end of the capsule so that a greater drying effect is experienced on the closed ends of the capsule than on the sides of the capsule. A plate is provided having multiple holes spaced 20 to match the position of the pins. The Oglevee patent discloses a method for insuring capsule wall thickness uniformity by measuring the viscosity of the liquid gel solution in the dipping tank and causing corrective change in viscosity by changing the evaporative exposure or by 25 adding lower viscosity gel to the tank. The Padilla patent discloses an air duct directing cooling air onto freshly dipped capsule mold pins for improved wall thickness characteristics. The duct is an air conduit for moving cool air upwardly against the rounded ends of the coated pins for 30 uniform flow. The duct encloses a zone surrounding the array of pins. The Lukas patent is directed to reducing the drying time in the manufacture of hard shell gelatin capsules. Pins are irradiated with microwave energy until the gelatin dries. The Lebrun patent discloses a dipping 35 bath, having a plurality of small wells and an impeller for maintaining the solution in the wells at a constant temperature. The pins dip into the wells.

- 6 -

Prior Art Capsule Forming Pins

U.S. Patent No. 4,758,149 to Sauter is directed to a capsule forming pin having a cylindrical sidewall and a groove extending around the cylindrical sidewall, the groove 5 having a non-angular cross-sectional profile, both the cylindrical sidewall and the groove having a smooth burnished-hardened surface. Sauter discloses in Fig. 3A, item C and column 4, line 45, that a prior-art capsule cap pin for a "0" ("zero") size capsule has a diameter at the 10 cut-point of 0.2973-0.2978 inch (7.551-7.564 mm). The prior-art capsule body pin at the cut-point is 0.2848-0.2853 inch (7.234-7.247 mm).

For a range of popular sizes of gelatin capsules, Table 4 shows the nominal cut-point diameter for the prior art 15 body pin and the prior art cap pin used in forming, respectively, the gelatin capsule body and the gelatin capsule cap.

PIN CUT-POINT DIAMETER					
20	Sizes	Body		Cap	
		Inches	mm	Inches	mm
	00	0.3195	8.12	0.3355	8.52
	0	0.2855	7.25	0.2975	7.56
	1	0.2575	6.54	0.2685	6.82
25	2	0.2355	5.98	0.2455	6.24
	3	0.2155	5.47	0.2255	5.73
	4	0.1955	4.97	0.2045	5.19

TABLE 4 - PIN CUT-POINT DIAMETER

- 7 -

Prior Art Process for Cellulose Capsules

An improved methyl cellulose ether composition that may be used in the present invention is disclosed in U.S. Patent No. 4,001,211 to Sarkar. Sarkar also discloses a process 5 for the manufacture of capsules from his improved methyl cellulose ether composition. The improved methyl cellulose ether composition disclosed by Sarkar is an aqueous solution of a thermal gelling methyl cellulose ether composition suitable for use in preparing pharmaceutical capsules by an 10 aqueous dip coating process using preheated pins and having a methoxyl DS of about 1.5-2.0, a C₂-C₃ hydroxyalkyl MS of about 0.1-0.4, a 2 wt. percent aqueous solution viscosity of about 2-10 cps at 20°C and a thermal gel point of about 50°- 80°C, and a 15-30 wt. percent aqueous solution viscosity of 15 about 1,000-10,000 cps at 20°C, said composition having as a 15-30 wt. percent aqueous solution: (A) essentially Newtonian fluid properties as defined by a power law coefficient, n, of 0.9-1.0 at shear rates of between 0.1-10 sec⁻¹, and (B) a 50 sec gel yield strength of at least 150 20 dynes/cm² at 65°C.

U.S. Patent No. 4,993,137 to Muto is directed to the manufacture of capsules made from the improved methyl cellulose ether composition of Sarkar. Muto discloses a process for gelling the solution by dipping solution-coated 25 pins into thermally controlled water. In the Muto process, the solution is gelled on the surface of the pins by first dipping the pins into solution and thereby coating the pins with solution and then dipping the coated pins into heated water to set the gel.

30 U.S. Patent Nos. 2,526,683 (to Murphy), 2,671,245 (to Kath), 3,617,588 (to Langman) and 3,842,242 (to Chisholm) are directed to methods of manufacture of capsules from methyl cellulose (the original methyl cellulose, not the improved methyl cellulose disclosed by Sarkar). The Murphy 35 patent is the original patent for the manufacture of methyl cellulose capsules. This patent discloses the preheating of pins prior to dipping so that the solution adheres to pins

- 8 -

in gelled form, the use of a sequence of different "successively warmer temperatures" through the drying kiln, drying using infrared lamps, and cooling by air. Murphy accomplished a mechanization for the manufacture of 5 cellulose capsules. However this method was found to be inadequate when (later) it was applied to the improved cellulose of the Sarkar patent. The Kath patent discloses apparatus for manufacturing either gelatin or methyl cellulose capsules. It discloses the use of tracks and a 10 plurality of pins. The pins are moved along the tracks and moved, rotated and gyrated as needed through the various stations. This patent contains detailed mechanical disclosure. The Langman patent is directed to elimination of unwanted thermal gelation in the coating bath by the use 15 of low viscosity hydroxyalkyl cellulose ethers and the rapid immobilization of the dip coating by induction heating after removal of the pins from the bath. The Chisholm patent is directed to heating the pins prior to dipping and discloses apparatus for preheating capsule pins in a 20 "Colton" capsule machine. A tray is provided containing spheroidal particles heated to a predetermined temperature. The pins are dipped into the heated particles just prior to being dipped in the solution.

The prior art for the manufacture of pharmaceutical 25 capsules from the improved thermogelling methyl cellulose ether compositions disclosed in the Sarkar patent contain a number of unresolved problems. These unresolved problems include skinning, wrinkling, starred ends and corrugations in the wall of the capsule parts, and damage to the capsule 30 parts occurring during removal from the pins. These problems cause breaking, failure to separate or jamming in the high-speed filling machines. There is no discussion in the prior art of the source of these problems.

None of the above mentioned patents disclose a method 35 for making cellulose capsules of sufficient uniformity and rigidity that they may be filled on modern high-speed capsule filling machines. This uniformity and rigidity has

now been accomplished using the process and capsule improvements that are the subject of the present invention.

Summary of the Invention

A method and apparatus for manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, uses an aqueous solution of a thermogelling cellulose ether composition and uses capsule body pins and capsule cap pins as molds. A group of pins is mounted on a bar. The method involves heating the pins; dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins; removing the pins from the solution; drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and removing the capsule bodies and capsule caps from the pins. In one embodiment of the present invention, the time interval between heating and dipping may vary from bar to bar. To compensate, each bar is heated to a different temperature according to the time interval associated with the bar. Pins may be heated by radiant energy or by hot air or via the bar at a plurality of thermally isolated stations. Additionally a portion of the bar may be heated to a predetermined temperature. The process includes heating the pins before dipping and heating the pins after dipping. The dipping dishes for capsule bodies and capsule caps are spaced apart farther than in the traditional Colton machine and a pre-dip heating area is located between the dipping dishes. After the pins have been dipped and removed from the solution they are heated again to further gelatinize the solution on the surface of the pins. Drying the pins includes providing counterflow movement of air through an enclosure over the pins such that the pins initially encounter relatively humid air and, as they become drier, they encounter increasingly drier air. Also, the pins are heated so that the capsule bodies and capsule caps are dried from the inside-out. Removing the capsule parts from the pins involves gripping the capsule parts between opposing gripping surfaces. In one embodiment the capsule parts have

- 10 -

a thicker wall than the equivalent size gelatin capsule and capsule bodies include a stiffening ring.

Problems in the prior art are overcome in one embodiment of the present invention as follows. In preheat, 5 to compensate for differential cooling from some bars waiting longer than others to dip, thermally isolated heating elements are provided below the bars and radiant heaters are provided above the bars to allow selective heating of bars or portions of bars to eliminate temperature 10 differences at the time of dip. To allow preheat in the dipper area without the problems associated with Chisholm's heated particle method, the dipping dishes are moved away from the centerline and thermal convection heaters and radiant heaters are inserted. For the same purpose, thermal 15 conduction heating via the back of the bars is also provided. To achieve the level of uniformity necessary for high-speed filling and to eliminate the skinning over and wrinkling associated with the outside-in drying of the prior art due to air blowing directly over the pins, inside-out 20 drying is provided. Post-dip heating is used in addition to pre-dip heating. Post-dip heating continues the gelling process after dip, assures rapid firming of the cellulose film, and supports inside-out drying. To avoid the uneven or excessively rapid drying that causes deformation in the 25 prior art, an appropriate relationship is maintained between water vapor pressure in the capsules and water vapor pressure in the surrounding air through the drying process. A fully enclosed drying kiln is provided to support inside-out drying, humidity control of air surrounding the pins, 30 and energy efficiency. To avoid damaging the open end of the capsule part during removal of the part from the pin, which often occurs when the prior art technique is used on cellulose capsule parts, a gripper is provided. To eliminate the jamming in the filling machines due to 35 oversize parts, the pin is undersized to compensate for the unexpected differential in shrinkage between the cellulose capsule and the gelatin capsule. To avoid malfunction in

- 11 -

filling machines caused by flexibility of the capsule part and deformation out of round, a pin is further undersized to allow a thicker capsule wall. Also the body pin adds an extra circumferential reinforcing ring to the capsule body
5 between the lock ring and the dome.

Brief Description of the Drawings

Figs. 1A, 1B and 1C show a prior art capsule body and cap.

Fig. 2 shows the elements of the traditional (prior
10 art) capsule manufacturing machine.

Fig. 3 shows pins mounted on a pinbar (prior art).

Fig. 4 shows a pin dipped to a dip line (prior art).

Fig. 5 shows a prior art stripper pushing a capsule part off a pin.

15 Fig. 6. shows a prior art stripper.

Fig. 7 shows a knife trimming the rough edge of the capsule (prior art).

Fig. 8A shows a schematic embodiment of the present invention, including a preheat section and a kiln enclosure.

20 Fig. 8B is a schematic cross-sectional elevation view of the drying kiln showing the enclosure and air flow.

Fig. 8C shows location of the heating elements and fans in the enclosure of Fig. 8B.

Fig. 8D shows a schematic plan view of all sections
25 between the split deck and the spinners.

Figs. 8E and 8F show two elevation views of the convection preheat system.

Fig. 8G shows the insulation box for the table section.

30 Fig. 9 shows a schematic embodiment of the present invention, including locations of the several preheat sections.

Figs. 10A and 10B show temperature sensors and under-deck heaters associated with the split deck.

35 Fig. 10C shows a group of cap pinbars and the corresponding group of body pinbars.

Fig. 10D shows the split deck layout for the bars of Fig. 10C.

- 12 -

Fig. 11 shows non-contact temperature sensors and overhead heaters associated with the split deck.

Figs. 12 and 13 show a plan and elevation view respectively of a dipper section preheat arrangement.

5 Figs. 14A and 14B show two views of a preheater with air ducts for selectively heating pins.

Fig. 15 shows the gel dish temperature control scheme.

10 Figs. 16A, 16B and 16C show apparatus for heating the pins through the pinbar to permit post-dip gelling in the spinner section and "inside-out drying" in the drying kiln.

Fig. 17 illustrates the process of removing the capsule part from the pin.

Fig. 18 gives detail of the stripper of Fig. 6 as modified for the present invention.

15 Detailed Description of the Invention

The present invention provides improvements over the method of manufacture of pharmaceutical capsules disclosed in U.S. Patent No. 4,001,211 to Sarkar. The Sarkar cellulose composition is particularly suited for preparing 20 pharmaceutical capsule shells which dissolve at a rate comparable to gelatin capsules. Delay release characteristics can be obtained by incorporation of a less water-soluble cellulose such as ethyl cellulose as described by Greminger and Windover in U.S. Patent No. 2,887,440. In 25 a preferred embodiment, the present invention uses the improved thermogelling methyl cellulose ether compositions disclosed in the Sarkar patent, including a thermal gelling methyl cellulose ether composition suitable for use in preparing pharmaceutical capsules by an aqueous dip coating 30 process using preheated pins and having a methoxyl DS of about 1.5-2.0, a C₂-C₃ hydroxyalkyl MS of about 0.1-0.4, a 2 wt. percent aqueous solution viscosity of about 2-10 cps at 20°C and a thermal gel point of about 50°-80°C, and a 15-30 35 wt. percent aqueous solution viscosity of about 1,000-10,000 cps at 20°C, said composition being further characterized by having as a 15-30 wt. percent aqueous solution: (A) essentially Newtonian fluid properties as defined by a power

- 13 -

law coefficient, n , of 0.9-1.0 at shear rates of between 0.1-10 sec⁻¹, and (B) a 50 sec gel yield strength of at least 150 dynes/cm² at 65°C.

The apparatus of the present invention, in a preferred embodiment, is based on the type of capsule machine disclosed in U.S. Patent No. 1,787,777 to Colton and U.S. Patent No. 2,671,245 to Kath. The machine that was modified to embody the present invention was a "Colton" capsule machine manufactured by R & J Engineering Corporation, 100 10 Hansen Avenue, Kitchener, Ontario, Canada N2C 2 E2.

1. General

The present invention provides a production process and a fully mechanized production apparatus that may use the modified cellulose in U.S. Patent No. 4,001,211 to Sarkar 15 for manufacturing pharmaceutical capsules of sufficient uniformity and rigidity that they may be filled on modern high-speed capsule filling machines. Capsules may be made in a range of sizes similar to the range of sizes in Tables 1-3. For a given capsule the capsule bodies and capsule 20 caps have different dimensions as illustrated for the prior art capsules in Figs. 1A-1C. The process involves a series of steps performed by one machine. Each capsule part is made by dipping a hot stainless steel pin into a cellulose gel solution and drying the gel to form a hard film over the 25 pin. The pins are mounted in a row on a bar as illustrated in Fig. 3. Fig. 4 shows a pin with a gel coating. Body pins are mounted on one set of bars and cap pins are mounted on a corresponding set of bars so that corresponding bodies and caps may pass through the entire process in phase with 30 each other and emerge from the process facing each other positioned for assembly as a capsule.

The process, in a first embodiment, is arranged so that the bars travel in a continuous loop illustrated in Fig. 8A. The process steps in this embodiment are:

- 35 Preheating the pin bars (Preheat Section);
 Oiling the pins (Greaser Section);
 Dipping the pins into cellulose solution (Dipper

- 14 -

Section);

spinning the coated pins (Spinner Section);

drying the gel (Upper and Lower Drying Kilns);

positioning the pinbars so that corresponding caps and

5 bodies face each other (Table Section);

removing the caps and bodies (Automatics);

trimming the caps and bodies (Automatics);

joining caps and bodies into prelock position
(Automatics).

10 Removing and trimming the caps and bodies is

illustrated in Figs. 17 and 7 respectively. Joining the
caps and bodies to form a capsule in a prelock position,
ready for filling, is illustrated in Figs. 1A and 1B. Fig.
1C shows a capsule with the lock ring engaged as it would be
15 after filling.

The process is similar to the process for manufacturing
gelatin capsules except that the process for manufacturing
gelatin capsules involves dipping cold pins into a gel whose
temperature is above the gel point whereas the process for
20 manufacturing cellulose capsules involves dipping hot pins
into a gel whose temperature is below the gel point. Novel
aspects of the present invention include process steps
designed to overcome the peculiar difficulties of
manufacturing cellulose capsules using the cellulose
25 composition disclosed in the Sarkar patent. In a preferred
embodiment, the present invention uses temperature, humidity
and air flow control components including heaters, sensors,
enclosures, fans and thermal isolation components. This
embodiment also uses pins that are narrower than the pins
30 used in the prior art and in one embodiment provides a
capsule body having a stiffening ring.

2. Temperature Control

Capsules must have consistent wall thicknesses from
capsule to capsule for them to be filled on high-speed
35 filling machines. To accomplish this, the temperature of
the stainless steel pin molds, which are attached to a
pinbar, must be controlled throughout the process. The pins

- 15 -

must be heated uniformly so that a repeatable amount of gel is picked up on each pin in the dipping operation. While several patents speak about the need to heat the pinbars prior to dip, none address the critical need for heating all 5 pins from bar to bar to substantially the same temperature to produce capsules sufficiently uniform for high-speed filling. In the process of making cellulose capsules on a traditional "Colton" capsule machine, some pinbars must wait longer than others to dip. The present invention includes 10 compensatory temperature control where some bars or parts of bars are independently heated to higher temperatures than others to compensate for the longer wait these bars have before dipping and for the different ambient temperature (due to temperature gradients within the machine) 15 experienced during the wait, and also for temperature gradients resulting from differing pin, pinbar, and/or deck conductivities. The compensatory temperature control system operates to maintain predetermined temperatures in the bars prior to dipping to achieve substantially equal temperatures 20 in the pins at the time of dipping. Compensatory temperature control can be provided by a variety of equipment configurations as follows:

- a) Compensatory Sensing and Heating on Drying Decks
Groups of twenty bars move from drying station to 25 drying station on a metal deck. Since bars sit in each position for some time before moving, heating sources may be positioned under the deck and also over the bars in such a manner so that heat may be applied to raise the temperature of selected bars in the group of twenty. The last station 30 of the lower deck, just prior to the table section, provides separate heating areas that are thermally isolated from each other so as to heat bars and portions of bars selectively. When bars leave the drying decks and load onto the table section, they are fed one at a time into the center elevator 35 for processing one at a time in the automatics section. The last bar in the group of twenty must wait the longest. By selectively heating these later bars to higher temperatures,

- 16 -

the delay before dip is compensated for. At time of dip, these later bars will have a temperature substantially equal to the earlier bars that had less time to cool down before entering the dipping station.

5 b) Insulation and Compensatory Heating in Table Section

After leaving the drying decks, bars are fed from the deck onto a Table Section which takes the group of twenty bars and feeds them one at a time into the T-slides for 10 continued processing. In this Table Section heat can be applied by any means to maintain the later bars at the required temperature so that they do not cool as they wait their turn for further processing. The table section is covered with an insulated box with heat sources to maintain 15 temperatures and further accommodate the later bars so that all bars reach the dipping bath at substantially the same temperature.

20 c) Compensatory Sensing and Heating to Adjust for Temperature Variations from the Front of the Bar to the Back of the Bar

Because of the temperature gradients within the machine, there is no guarantee (with the prior art machines) that the temperature along the length of a given bar will be constant. Variation of temperature along the length of the 25 bar would cause temperature variation pin to pin. For example, the front end of the bar may be cooler than the back end, and thus pins in the front are also cooler. In the present invention, the differential heating mentioned above also may be set up to compensate for temperature 30 gradients within the machine in order to ensure uniformity of temperature, pin to pin, along a given bar. This is accomplished by applying heat selectively via the deck supporting the bars and from overhead radiant heaters. The last station of the lower deck, just prior to the table 35 section which delivers bars one at a time to the automatics, is known as the "split deck." Heating from each thermally isolated segment of the split deck is adjusted to produce a

predetermined temperature profile that results in the temperature of all pins being equal when they reach the dipper.

3. Novel Approaches to Drying Cellulose Capsules After the
5 Dipping Process

a) Counterflow Drying and Enclosed Kilns

Drying techniques used in prior art mechanized capsule manufacture involves overhead kilns with perforations on the bottom plate through which air blows over the capsules. The 10 air then escapes into the room. The present invention uses enclosed kilns where air is only introduced at the pin-exit end of the lower kiln (i.e., the end of the drying process) and then proceeds in a counterflow direction to the pinbar movement, all air being contained in the enclosed kilns and 15 being removed at the pin-entry end of the top kiln, which is the beginning point of the drying process. The pins, on entering the drying process, encounter relatively humid air and, as the pins move through the drying process and become drier, they encounter increasingly drier air.

20 b) Inside-Out Drying

All capsule drying was formerly accomplished by drying from the outside by blowing air over the pins from above. The present invention dries from the inside-out by using heat both from beneath the deck and also from above the pins 25 (radian or infrared, microwave, etc.) to heat the pins themselves, thus driving the moisture out from the inside. This gives more uniform capsules free from defects of wrinkles and corrugations common with outside-in drying, and avoids the case hardening or skinning over that occurs in 30 cellulose capsule production by drying with air alone.

4. Novel Ways to Preheat Pinbars Prior to Dipping

a) Adding a Separate Preheat Section to the Process Prior to Dip

Heating the pins is necessary so that gel will be 35 formed on the pins in the dipping bath. In the Murphy patent, pins are heated as a byproduct of the drying. The hot air used to dry the capsules also heated the pinbars (in

a way that is uncontrolled with regard to pin-temperature requirements for dipping) before capsule removal and redipping. The only mention in the prior art of controlled preheating is the Chisholm patent which suggests that the 5 pins be immersed in a bath of hot beads prior to dip. In practice the Chisholm approach is not feasible because of the problems discussed hereinbelow under "Analysis of the Problems in the Prior Art." For example, removal of capsules made from the improved cellulose from pins is even 10 more difficult than removal of capsules made from gelatin from pins (also very difficult) because the improved cellulose forms a weaker and more flexible film. Because the walls of the capsule parts lack sufficient rigidity to be removed easily, the lubricant layer must be administered 15 carefully and left intact. The present invention provides a preheat area whose specific purpose is to apply heat to the pins without contact in preparation for dipping. This preheat area can be in any or all of the following places:

- a) On the drying decks, or at the end of the drying 20 decks and before the table section.
- b) On the table section.
- c) Between the table section and the automatic section.
- d) After the automatic section and before the 25 greasing section.
- e) After the greasing section and before the dipping section by means that do not contact the pins.
- f) In the dipping section by means that do not 30 contact the pins, such as radiant heat, hot air, induction heat, contact elements to back side of bar, or other suitable method. Another problem with the Chisholm approach is that the traditional capsule machine does not have room to accommodate the procedure he recommends because of the close proximity of the dipping dishes to the centerline of the machine. Thus the present invention also 35 includes extending the dipper section on both cap

- 19 -

and body sides to move the dipping dishes further out from the centerline of the longitudinal axis of the traditional capsule machine. This allows space to accommodate a preheat process that does
5 not involve contact with the pins.

5. Description of Apparatus

Fig. 8A shows some elements of a first schematic embodiment the apparatus of the present invention, most notably a preheat section 80, a kiln enclosure 81, with air 10 ingress aperture 82 and air egress aperture 83, an insulated, heated table section enclosure 84, an insulated, heated spinner section enclosure 85 and a dipper section having a built-in preheat portion 86. The arrows in Fig. 8A indicate the direction of pin movement through the machine.

15 Fig. 9 shows a schematic embodiment of the apparatus of the present invention including several preheat sections, as follows: in the drying kiln 80, between the drying kiln and the table section 91, on the table section 92, between table and automatics 93, between automatics and greaser 94, 20 between greaser and dipper 95, and in the dipper section 96.

Fig. 8B shows the overall physical shape of kiln. The overall length L1 of the machine, i.e., the length of the upper kiln, is 44 feet (13.4 m). This is longer than the traditional Colton machine, the upper kiln having been 25 extended by three table-lengths to accommodate a new preheat section 94 (shown in Fig. 8C) between the automatics and the greaser. The height H1 of the upper kiln is 2 feet (61 cm). The length L2 of the lower kiln is 26 feet (7.9 m). The height H2 of the lower kiln at the split deck is 2 feet (61 30 cm) and the height H3 of the lower kiln at the back elevator is 1 foot (30 cm). The walls of the kiln are insulated. The kiln comprises an enclosure 81 having air entrance duct 801 and air exit duct 802. The direction of air flow is indicated by arrows 803. Fig. 8C locates the two 6-inch 35 (152-mm) circular duct fans 805 and the single 10-inch (254-mm) duct fan 807, all mounted in the lower kiln 26, which power the air flow though both kilns. The two duct fans 805

- 20 -

are mounted side by side so as to blow air in a direction substantially parallel to the axis of the lower kiln toward the back of the machine, drawing air from inlet 801 and driving it into the upper kiln 24. Eight 9-inch (229-mm) agitator fans 804 in the upper kiln are arranged in four pairs of side by side fans, each pair directed to blow air downwardly onto the pins so as to speed local drying of the gel with agitated (i.e., temperature-equalized) air. Three 9-inch (229-mm) fans 806 similarly mounted in the lower kiln dry the pins further.

Heat for inside-out drying and preheat is supplied by a series of five 22 inch by 17 inch (56 cm by 43 cm) radiant panels 808 mounted directly above the moving pinbars in the lower kiln. General preheat of the pinbars in the split deck position is provided from above by a 22 inch by 17 inch (56 cm by 43 cm) group of radiant panels 809 directly above the pinbars and preheat is applied selectively to portions of pinbars by conduction from the split deck assembly 810 that supports the pinbars. A "dome-setter" radiant panel 811 is provided for post-dip heating to facilitate post-dip gelling and inside-out drying.

The fan and heater configuration described above applies to one side, cap or body, and, in this respect, the cap and body sides are substantially identical, except that they are the mirror image of each other.

Inlet air temperature to the kiln is controlled in the range 125-180°F and is preferably 160°F. Absolute humidity of the air at the inlet is controlled in the range 0.006-0.012 lb moisture/lb air (0.6-1.2 percent) and is preferably 0.009 lb moisture/lb air (0.9 percent). Air flow rate through the body side of the kiln is 63 feet/min (0.32 m/sec) measured at the 8 inch (203 mm) body side inlet duct. The corresponding flow rate through the cap side kiln measured at a cap side inlet duct of the same size is 7 feet/min (0.036 m/sec). Within the kiln the flowing air is cooled by evaporative cooling and is heated by heat from the bars and from the radiant panels. The temperature profile

- 21 -

found to provide acceptable capsule parts is given in Table 5. Heat from the radiant panels and thermal conduction heaters is adjusted to maintain the predetermined temperatures of Table 5. Pressure drop across the kiln is 5 0.020 inches of water (0.005 kPa) (body side) and 0.005 inches of water (0.012 kPa) (cap side). This indicates how much greater the air flow rate through the body side is than the air flow rate through the cap side.

10

15

20

25

Location in Kiln	Body Kiln		Cap Kiln	
	°F	°C	°F	°C
A	111	43.9	111	43.9
B	109	42.8	108	42.2
C	110	43.3	107	41.7
D	110	43.3	106	41.1
E	111	43.9	104	40.0
F	114	45.6	104	40.0
G	120	48.9	105	40.6
H	123	50.6	112	44.4
I	142	61.1	140	60.0
J	151	66.1	159	70.6
K	149	65.0	147	63.9

TABLE 5 - ACCEPTABLE AIR TEMPERATURE PROFILE

Figs. 10A and 10B show temperature sensors and under-deck heaters for preheat on the split deck in the drying kiln. Figs. 10A and 11 give details of split deck 810 and 30 radiant panel 809 respectively from Fig. 8C. Fig. 10A shows sensors 104 mounted in deck 101. Heaters 103 are mounted under the deck. Both sensors and heaters are electrically connected to controllers 105 which maintain the predetermined temperatures given in Tables 6A and 6B. The 35 deck itself contains thermal isolators 102, so that the

- 22 -

several sections of deck beneath a given pinbar are thermally isolated one from another. Cap pinbars move in groups of twenty from station to station approximately every 40-70 seconds in the drying kilns and body pinbars do 5 likewise. The direction of movement of the pinbars is shown by the arrows in Fig. 10C. Such a group of pinbars has a length of 22 inches (56 cm), the length of one pinbar, and a width of 17 inches (43 cm), the width of twenty pinbars. Supporting the pinbars in the last station of the drying 10 kiln is the split deck shown in plan view in Fig. 10D. The thermal isolators 102 and the portions of the deck 101 enclosed by the thermal isolators are also shown in cross-section elevation view in Fig. 10A. Selective heating of different portions of twenty pinbars to compensate for pre- 15 dip dwell time and for temperature gradient in the machine is achieved by controllers 105 controlling each of the several enclosed deck portions at a predetermined temperature. A temperature profile for a preferred embodiment of the present invention is given for each 20 enclosed deck portion 101 of Fig. 10D in Table 6A for the cap side and Table 6B for the body side. The dimensions of the enclosed deck portions 101 in Fig. 10D are given in Table 6.

	A °F (°C)	B °F (°C)	C °F (°C)	D °F (°C)
1	306 (152)	251 (122)	235 (113)	267 (131)
2	181 (82.8)	178 (81.1)	153 (67.2)	174 (78.9)
3	193 (89.4)	165 (73.9)	135 (57.2)	142 (61.1)

30 TABLE 6A - CAP SIDE SPLIT DECK TEMPERATURE PROFILE

- 23 -

	A °F (°C)	B °F (°C)	C °F (°C)	D °F (°C)
1	246 (119)	191 (88.3)	252 (122)	288 (142)
2	213 (101)	125 (51.7)	193 (89.4)	154 (51.1)
3	209 (98.3)	195 (90.6)	273 (134)	261 (127)

5

TABLE 6B - BODY SIDE SPLIT DECK TEMPERATURE PROFILE

	A Inch (mm)	B Inch (mm)	C Inch (mm)	D Inch (mm)
1	3 x 4 (76 x 102)	5 x 4 (127 x 102)	5 x 4 (127 x 102)	3 x 4 (76 x 102)
2	3 x 10 (76 x 254)	5 x 10 (127 x 254)	5 x 10 (127 x 254)	3 x 10 (76 x 254)
3	3 x 4 (76 x 102)	5 x 4 (127 x 102)	5 x 4 (127 x 102)	3 x 4 (76 x 102)

- 10 15 Fig. 11 shows non-contact temperature sensors and overhead radiant heaters for general preheat on the split-deck in the drying kiln, detail 809 of Fig. 8C. Non-contact sensors 111 measure the temperature of the pins (or local area of pinbar) from above. Overhead radiant heaters 112 are mounted to the thermal enclosure 113. Controllers 106 are used (in conjunction with controllers 105) to maintain the predetermined temperatures of Tables 6A and 6B on the split deck.
- 20 25 Additionally, hot air may be used for heating in the split deck area.

Fig. 8G shows the insulation box 831 for preserving preheat in the table section 27. The box has a top and only two sides, one side being omitted to allow a group of twenty bars to enter and another side being omitted to allow bars 30 to exit (in a direction transverse to their length) one at a time.

Fig. 8C locates (schematically) the table section 27,

- 24 -

the automatics 28, the convection preheat section 94, the greaser section 21, the dipper section 22 and the spinners 23. The convection preheat section 94 includes up to three convection heat systems 812 on each side. Arrows 813
5 indicate the direction of flow of heated air across the pinbar after the pinbar has left the automatics where capsules were removed and before the pinbar enters the greaser section 21 and the dipper 22. The location of each of the six convection preheat systems 812 is shown in Fig.
10 8D between automatics 28 and greaser section 21. The convection preheat system is shown in greater detail in Figs. 8E and 8F. Fig. 8E shows the squirrel cage blower 821, the heating element 822, the supply duct 823, the pinbar 824, the pin 825 and the return duct 826. To
15 accommodate the convection preheat section 94, the original Colton machine was extended by three table-lengths, i.e., the upper kiln was extended by three table-lengths and the greaser section was moved three table-lengths away from the automatics. In a preferred embodiment, four convection
20 preheat systems are used, two on each side. Fig. 8D also shows a schematic plan view of all sections between the split deck 810 and the spinners 23, including the accumulators 832 and the final preheat section 95, whose location necessitates that the dishes are located farther
25 apart than they are in the traditional Colton machine.

Lubrication used in the greaser section 21 consists of a mixture of light mineral oil (59 percent), stearic acid (16 percent), calcium stearate (16 percent), and lecithin (9 percent). A very small measured quantity is delivered by a
30 metering pump to a felt or brush which applies the lubricant directly to the pins. Then a felt-lined barrel distributes the lubricant uniformly over the pin surface.

Figs. 12 and 13 show a plan and elevation view respectively of a dipper section preheat arrangement. There
35 is symmetry about line A-A except that capsule bodies are on one side and capsule caps are on the other. Body pinbars and cap pinbars slide into the dipper section preheat area

- 25 -

in T-slides 121 and drop onto guide rails 124. The dipper dishes are spaced apart to allow an area for the final preheat section 95. See also Fig. 9. Heated air is blown across the pinbars via inlet ducts 123 and preheat hoods 122. The pinbars, leaving the preheat area, are dipped in groups of five in the dipping dish 125 and spun in the spinners 23 within an enclosure 161.

Fig. 13 shows a group of five bars in the accumulator 832 (five bars having fallen from the T-slides one at a time until five bars are accumulated in the accumulator). This group of five bars moves to station 131 in the final preheat 5 section 95 where final preheat is applied. In an alternative embodiment, one that eliminates the need for preheating pins according to a time interval to compensate for different delay times between preheat and dipping, the dishes are moved apart further to accommodate a sufficient 10 number of stations 131. In this embodiment all preheat is performed between the accumulator and the dishes and is performed without disturbing the layer of grease that was applied to the pins on the greaser. Heat is preferably applied by thermal convection from hot air flowing over the 15 pins as shown in Fig. 13, or by radiant heat. Heat may also be applied by moving a conducting bar into contact with the top surface of the bars, the pins pointing down as shown in Fig. 13. Alternatively, induction heating may be used.

Figs. 14A and 14B show two views of a preheater with 20 air ducts for selectively heating pins in the T-Slides. Air for heating the pins passes through supply ducts 141 and return ducts 142. The local temperature of the pinbar is measured by non-contact sensor 143. This is an alternative to the convection preheat section of Figs. 8E and 8F.

25 Fig. 15 shows the schematic for control of the dish temperatures. Water 157 is pumped by circulating pump 151 through a chiller 152 and a heater 153. The heater is controlled by a PID controller 154 connected to a temperature sensor in the body dish 155. After the water 30 leaves the heater, it flows through jackets around both the

- 26 -

body dish 155 and the cap dish 156. The temperature in both dishes is controlled to 81°F ±1°F (27.2°C ±0.6°C). Body pins should enter the dish at a temperature of 152°F (66.7°C) (range 144°F-156°F (62.2°C-68.9°C)) and cap pins at 5 a temperature of 151°F (66.1°C) (range 149°F-156°F (65.0°C-68.9°C)). After a pin has been dipped, its temperature should be in the range shown in Table 8.

	Temperature		Optimum °F (°C)	Minimum °F (°C)	Maximum °F (°C)
10	<u>Location</u>				
	Table Load (Spinner)	Body	124 (51.1)	123 (50.6)	126 (52.2)
15		Cap	122 (50.0)	121 (49.4)	124 (51.1)
	Table 1 of Upper Deck	Body	----	119 (48.3)	121 (49.4)
		Cap	----	120 (48.9)	124 (51.1)

TABLE 8 - PIN TEMPERATURES AFTER DIPPING

Figs. 16A, 16B and 16C show apparatus for heating the 20 pins through the pinbar to permit post-dip gelation in the spinner section and "inside-out drying" in the drying kiln. The spinner section is enclosed and heat is applied to the pins to cause continued gelation and inside-out drying. Heat is applied in the spinner section by blowing hot air 25 over the pins via ducts 163 and 164 and by heating the pins from radiant panels 162 mounted to the walls of the enclosure 161. Panels 162 are substantially parallel to the longitudinal axes of the bars. It has been found that using 30 a pin temperature at dipping that is cooler than the temperature used by Murphy, and heating the pins after dipping to continue gelation, provides a better consistency and fewer defects in the finished capsule. Heat applied to the pinbar in the drying section drives moisture from the inside-out as shown in Figs. 16B and 16C (inside-out 35 drying). Arrows in Fig. 16C in the bar and pin indicate

flow of heat. Arrows in Fig. 16C in the gel and in the air indicate flow of moisture. Inside-out drying prevents the formation of "skin" on the outer surface of the capsule that can occur when drying from the outside with blown air alone.

5 Fig. 17 illustrates the process of removing the capsule part from the pin. A gripper 171 (modified stripper) pivots about pivot 172, when driven by wedge 173, to grip the capsule part 174 prior to sliding it off the pin. The gripper has opposed gripping faces.

10 Fig. 18 gives details of the gripper of Fig. 6. The gripping faces 181 may be provided with raised ridges or rows of teeth (which may be longitudinal or circumferential to the axis of the pin), or have surface composition or texture, so as to grip the capsule.

15 6. Pin Size

An important factor in achieving production quantities of capsule bodies and caps that will run problem-free in high-speed filling machines is to meet close specifications, especially on external dimensions. For example, if the 20 external diameter of each capsule part is even slightly too large, caps and bodies will not consistently separate in the filling chamber because they are too tight a fit. The external diameter of a capsule part is determined by the diameter of the pin mold, the shrinkage of the capsule 25 material after removal from the mold, and the thickness of the capsule wall. The thickness of the capsule wall depends on a number of factors including the initial moisture content and viscosity of the gel and the drying conditions. Accordingly, it is recommended, for the manufacture of a 30 cellulose capsule part, to use a pin whose diameter is undersized compared to the capsule pin for the corresponding size gelatin capsule part. For example, for the manufacture of a "0" size cellulose capsule part it is recommended to use a capsule pin whose diameter is undersized by an amount 35 in the range of approximately 0.002-0.006 inch (0.05-0.15 mm) or approximately 0.004 inch (0.1 mm) compared to the capsule pin for manufacture of a "0" size gelatin capsule

- 28 -

- part. For other capsule sizes, it is recommended that the pin diameter be undersized proportionately. From Table 4, the cut-point diameter of the prior art capsule cap pin is 0.2975 inch (7.56 mm) so a reduction range of 0.002-0.006
5 inch (0.05-0.15 mm) represents a reduction range of 0.7%-
2.0% and a reduction of 0.004 inch (0.1 mm) represents a
reduction of 0.13%. For forming capsule parts for capsules
having thicker walls and the same external diameter, the pin
diameter may be reduced further as discussed under
10 "Increasing Capsule Stiffness" hereinbelow.
7. Cooling the Dipping Dishes
- Passive cooling was found to be insufficient to dissipate the heat delivered to the dipping dishes by the entry of a succession of hot pins. In the prior art
15 machines used to make gelatin capsules this problem cannot arise because cold pins are dipped into a hot gel. In these prior art machines, a jacket having pipes is used to pass hot water to maintain the temperature of the dipping dishes. A similar jacket is used in the present invention except
20 that in the present invention the jacket is used for cooling. The jacket includes pipes that carry cooling water for removing heat from the dipping dishes so as to control the temperature of the solution in the dipping dishes and the maintain the solution at a substantially constant
25 predetermined temperature.

8. Increasing Capsule Stiffness
- Cellulose capsules made from the improved methyl cellulose ether composition disclosed by Sarkar are found to be less rigid than gelatin or earlier cellulose capsules of
30 an equivalent shape, size and wall thickness. Also, it is essential that the capsule parts retain their shape in order to pass freely through the high-speed filling machine. For these reasons it has been found beneficial to increase the wall thickness of the capsule parts without increasing the
35 external diameter of the capsule. (The external diameter of the capsule is the external diameter of the capsule cap.) Increasing the wall thickness for a given capsule size is

- 29 -

accomplished by using a thinner cap pin, a thinner body pin and a combination of hotter pin and/or thicker solution. Other factors which may be used to increase wall thickness are longer dwell time in the dipping dishes, more time in 5 the downward position in the spinning section and a modified temperature profile in the gelling stage. For a "0" size capsule, a wall thickness increase of approximately 0.0005 inch (0.013 mm) is recommended, yielding a wall thickness of a capsule cap of approximately $(0.0042 + 0.0005) = 0.0047$ 10 inch (0.119 mm). To increase the wall thickness of a capsule cap by an additional dimension Δw without increasing the external diameter, it is necessary to reduce the diameter of the cap pin by approximately $2 \times \Delta w$. To make the corresponding capsule body it is necessary to reduce the 15 diameter of the body pin by approximately $4 \times \Delta w$ so that the body will fit into the smaller inside diameter of the cap. Accordingly, for a "0" size cellulose capsule having a wall thickness as recommended, the cap pin diameter is reduced by 0.001 inch (0.026 mm) and the body pin diameter is reduced 20 by 0.002 inch (0.052 mm) in addition to the reduction discussed hereinbelow under "Capsule External Diameter and Pin Mold Diameter." From Table 4, the cut-point diameter of the prior art cap pin is 0.2975 inch (7.56 mm), so an additional reduction 0.001 inch (0.026 mm) represents an 25 additional reduction of 0.3%. Again from Table 4, the cut-point diameter of the prior art body pin is 0.2855 inch (7.25 mm), so an additional reduction of 0.002 inch (0.052 mm) represents an additional reduction of 0.7%.

Alternatively, or additionally, the stiffness of the 30 capsule may be increased by providing in the capsule body a reinforcing ring, similar to the locking ring, located between the locking ring and the dome of the capsule body. This approach provides, for a given capsule wall thickness, a stiffer capsule with a reduced penalty in terms of 35 material content of the capsule body and reduction in interior volume of the finished capsule. One or more reinforcing rings may be provided.

- 30 -

9. Serial Dipping

An alternative embodiment of the present invention uses serial dipping of pins instead of the batch dipping using a modified Colton machine as described hereinabove. Serial dipping permits every pin to proceed through an identical preheat process. This eliminates the need to compensate for different elapsed time pin-to-pin between preheat and dipping. Dipping one pin at a time would, of course reduce the throughput rate by a factor of 150 over the embodiment of Fig. 8A in which there are thirty pins per bar and five bars are dipped together as a batch. However, it would be possible to mount pins on an articulated base (i.e., a chain) one pin per link, and circulate several such chains in parallel through a preheat process, a dipping process and a drying process on a machine, including an enclosed drying kiln, designed for the purpose. Another alternative embodiment of the present invention provides multiple pins on a bar and transports one bar at a time through both the preheat section and the dipping section. In this way the bar-to-bar difference of elapsed time is eliminated and only the differential temperature along the bar must be compensated. This could be accomplished by a functional equivalent of the split deck.

Solutions to the Problems Unresolved in the Prior Art

25 A. Analysis of the Problems in the Prior Art

An important contribution of the present invention is the analysis of the several unresolved problems in the prior art from the perspective of each stage of manufacture and use, as follows:

30 A1. Preheat

In the Colton machine the most acceptable areas for preheating are those prior to the table section where the bars are assembled in groups of twenty and are stationary for a period during which they can all be heated together.

35 However, the problem with preheating prior to the table section is that the action of the table section causes some bars to wait longer than others for their turn to dip and

- 31 -

this can result in some bars cooling more than others prior to dipping, with the cooler bars making thinner capsule walls than the other bars. Also, the pins on one end of the bar might be hotter or cooler than the pins on the other end 5 of the bar simply due to temperature gradients across the machine.

An appropriate place to heat the bars is in the dipper section just prior to dipping. In that section of a traditional Colton dipping capsule machine, five or more 10 bars are grouped together and then moved as a group over to the dish for dipping in the gel solution. This allows for simultaneous heating of a group of bars which avoids the waiting problem identified above. The only patent to address preheating bars in the dipper portion of the Colton 15 machine is Chisholm. In the Chisholm patent, pins are dipped into heated particles which contact the pins directly, heating them to the appropriate temperature for dipping. This approach creates other problems. First, the lubricant coating on the pin prior to dipping is important 20 because cellulose capsules are much more difficult to remove from the pins than gelatin. Since the lubricant is already applied at this point in a Colton style capsule machine, the use of a pin-contact heating method results in unreliable capsule removal due to disturbance of the lubricant layer. 25 Second, there is the problem of lubricant continuing to accumulate in the bead particles, degrading in the heated particles, and being redeposited on the pins at a later time. Third, there is no room in a traditional Colton machine to accommodate such a heated particle device. 30 Fourth, no method of preheating alone (as opposed to pre-and post-heating) has been successful in making capsules from the Sarkar improved cellulose of sufficient uniformity for high-speed filling.

A2. Capsule External Diameter and Pin Mold Diameter

35 For any given standard size of capsule (such as "0", "1", "2", etc.), the size of the pin mold used in the prior art is a well accepted standard with little variation in

- 32 -

size. The combination of the standard pin mold diameter, accepted standards of wall thickness, and shrinkage contribute to an overall dimensional standard for the outside diameter of a capsule of a given size which can be 5 accommodated without difficulty on high-speed filling machines where tolerances are tight.

The prior art teaches that the same pin mold may be used for cellulose as is used for gelatin, and there is no prior art that has stated otherwise. However, using the 10 prior art pin for a given capsule size makes a cellulose capsule that is often oversized compared the given standard size capsule. This causes difficulties in the high-speed filling machines.

A3. Drying

15 The traditional drying kilns in the prior art employ plates with holes above the pins to introduce a stream of air in proximity to the capsules (Wilkie). Blowing air over the pins causes evaporative cooling which works well with gelatin since the cooling helps set the gel. However, with 20 cellulose the object is to keep the gel above its thermal gel point until it is thermally set to a sufficient firmness. The traditional (Wilkie) design cools the wet cellulose gel through evaporative cooling, and can cause the gel to flow unevenly and uncontrolled down the mold pin. 25 This makes an uneven capsule which cannot be filled on the precise high-speed filling machines.

Further, while some air movement is necessary to remove water vapor released during drying, air movement has a tendency to deform capsules made of cellulose more 30 drastically than capsules made of gelatin, and a directed stream of air over the capsules can shift the gel before it is firm.

Blowing air over the exterior of the pins also causes the gel to dry from the outside first, causing a "skin" to 35 form which traps moisture inside the film. This can lead to wrinkles or corrugations of the capsule wall, and subsequent problems on high-speed filling machines. Murphy employed a

drying design similar to the Wilkie plates, but his patent concerns methyl cellulose which is slower drying and less apt to surface harden. The modified cellulose indicated in the Sarkar patent has a tendency to dry faster and is prone
5 to deformation when dried in the conventional way.

Experimental work done by Eli Lilly with the improved Sarkar cellulose showed that conventional drying design with plates and holes has a tendency to cause starred ends and corrugations of the capsule walls. This is a result of
10 compromise in the cellulose formulation, which improves dissolution (in the human digestive system) but results in faster release of moisture compared to celluloses used in earlier capsule technology.

Higher temperatures are used in the cellulose drying
15 process than are used in the gelatin drying process. In the prior art drying process, air blows over the pins and escapes to the room. With the higher temperatures of the cellulose drying process, this adds significant heat and heating loads to the room and requires costly air
20 conditioning.

A4. Capsule Removal

With the improved cellulose in the Sarkar patent, removal of the capsule from the pin mold is one of the most difficult problems. The traditional approach used before
25 the present invention involved a clothespin like device, called a stripper. The stripper traveled over the dipped length to a position beyond the capsule part. It then closed on the bare pin and moved along the length of the pin until it contacted the edge of the capsule and subsequently
30 pushed the capsule part off the pin.

The improved cellulose lacks the rigidity necessary for a clean release from the pin when contacted by the stripper cheek. There is a tendency for the cellulose part to continue to adhere to the pin and to deform and break under
35 stripper pressure rather than releasing freely.

A further complication in stripping cellulose capsules is the low moisture content. Whereas moisture can aid

- 34 -

capsule removal in the gelatin process, cellulose capsules become soft at even modest moisture levels. Thus stripping must always be accomplished under dry capsule conditions. As with gelatin, dry capsules make capsule removal more 5 difficult.

Increasing lubrication to aid stripping also poses problems since the cellulose gel is very prone to movement during and immediately after the dip. Excessive lubrication, or even lubricants with particularly slippery 10 characteristics, have a tendency to cause uneven capsule walls. High temperatures inherent in the process add other constraints to the choice of lubricant.

A5. Capsule Filling

Lack of uniformity, the sources of which are discussed 15 hereinabove, causes problems on high-speed filling machines. In addition, the flexibility of the improved Sarkar cellulose also causes another problem: being flexible, the capsules are easily deformed out of round.

B. Solution of the Problems in the Prior Art

20 The problems in each stage of making and using the capsules are solved in the following manner:

B1. Preheat

Since some bars must wait longer than others to dip, the present invention addresses the issue of differential 25 cooling and temperature compensation by selectively heating some bars to a higher temperature than other bars so that all bars have substantially the same temperature when dipped as a group of five or more. This is accomplished by using a pattern of thermally isolated heating elements below the 30 bars (the "split deck") and above the bars (radian heaters). These heating elements selectively heat certain bars to predetermined temperatures so that substantially equal temperatures are achieved at dip.

In addition, the temperature of a bar may vary along 35 its length or front to back. The split deck allows the selective heating of portions of bars, those portions which are otherwise repeatedly cooler than other portions.

Thermal sensors are used to maintain the individual heating areas at an appropriate temperature to consistently deliver all bars and portions of bars at substantially the same dip temperature.

- 5 Preheating in the dipper section may be accomplished by heating the pins by a non-contact heating method which overcomes the problems associated with Chisholm's heated particle method. Hot air, radiant elements, etc. may be used in proximity to the pins without disturbing the
10 lubricant layer, and without the concern of deposits of lubricant on the contact particles. To accommodate non-contact preheating in the dipper just prior to dip, the present invention modifies the Colton style machine by extending it away from centerline on both the cap side and
15 the body side. Also, contact to the back of the bars (away from the pins) may be used to aid preheating in the dipper. Heated elements may be moved directly in contact with the back of the bars as sole preheating, or in conjunction with a non-contact heating method applied to the pin side of the
20 bar.

To achieve the level of uniformity necessary for high-speed filling, pre-dip heating and post-dip heating are used in conjunction. Post-dip heating continues the gelling process after the dip and assures rapid firming of the
25 cellulose film. This is accomplished by applying heat directly before the dip and directly after the dip and continuing to apply heat for gelation and inside-out drying until the film is sufficiently firm.

B2. Capsule External Diameter and Pin Mold Diameter

- 30 The apparatus of the present invention includes a pin mold which is undersized to compensate for the differential in shrinkage between capsules made from the improved cellulose composition and capsules made from gelatin. This results in a cellulose capsule which has the same overall
35 diameter and wall thickness as the equivalent gelatin capsule, and is therefore capable of running in existing high-speed filling machines.

B3. Drying

The present invention does not use plates with air blowing directly over the pins, but uses a fully enclosed drying tunnel (kiln), in which drying is accomplished by 5 inside-out drying in the most critical stages of drying. This is accomplished by using heating elements directly under the deck (or bottom) of the drying tunnel and radiant elements overhead in the drying tunnel, keeping pins above the thermal gel point of the cellulose in the early drying 10 stages. This drives moisture out from the inside. It avoids the skinning over and wrinkling associated with the outside-in drying of the prior art.

Process air is directed through the enclosed drying tunnel in counterflow to the direction of motion of the 15 pins. The purpose of the counterflow air is not so much to dry the capsule walls, but rather to move moisture through the system which has been driven out of the capsule parts by inside-out drying so the moisture can be exhausted from the drying kilns. In this procedure, drier capsules at the end 20 of the drying tunnel come into contact with dry air which is introduced at the end of the drying tunnel. As the air moves towards the beginning of the drying tunnel, it picks up moisture. Therefore, wet capsules at beginning of the drying tunnel come into contact with wet air and drier 25 capsules at the end of the drying process come in contact with drier air. This keeps an appropriate relationship of water vapor pressure between capsules and throughput air throughout the drying process to ensure even drying. The result is a capsule part without deformation.

30 In addition, local heating or air agitation is employed to speed drying in selected areas where the film is sufficiently firm so that deformation is not a problem. Full enclosure and insulation of the drying kilns also prevents heat escaping into the room, thereby avoiding the 35 higher heating load on the facility that would occur without full enclosure. This is in direct contrast to the prior art, in which not air is blown over the capsule parts and

then escapes into the room.

B4. Capsule Removal

Murphy used the non-modified cellulose, which was rigid enough to be removed by traditional methods. However, the

- 5 improved dissolving cellulose of Sarkar cannot be consistently removed by pushing capsule parts off the pin by pushing from behind the dipped edge. In the present invention, the "stripper" device is modified into a gripper, which has two opposed surfaces which grab the capsule above
- 10 the dipped edge, on the capsule wall itself, and remove the capsule using pressure to the side walls in conjunction with a motion along the longitudinal axis of the pin mold. The Colton machine is modified to allow the grippers to open wider than normal strippers and the machine is also modified
- 15 to move the gripper into a position closer to the closed end of the capsule so that it contacts on the capsule surface, rather than behind it. This action removes the capsule without damage to the open end, which often occurs when the prior art technique is used on cellulose capsule parts.

20 B5. Capsule Filling

The flexibility of capsules made from the improved cellulose can cause capsules to malfunction in filling machines, particularly if deformed out of round. The apparatus of the present invention provides a pin which is

- 25 undersized (in the correct amount) to allow a thicker capsule wall, and therefore better rigidity, while maintaining the accepted overall diameter of a given standard capsule size, such as "0", "1", etc.

- The apparatus of the present invention also provides a
- 30 body pin which adds an extra circumferential ring to the capsule body between the lock ring and the dome which physically reinforces the capsule wall. One or more extra rings may be added to increase the overall strength of the capsule body part, and to assure capsule bodies remain
 - 35 circular.

What is claimed is:

1. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as molds, comprising:
 - heating the pins;
 - dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins;
- 10 removing the pins from the solution;
- drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and
- removing the capsule bodies and capsule caps from the pins;
- 15 wherein the step of heating the pins includes heating a pin to a predetermined temperature that is determined in accordance with the expected time interval between the step of heating the pin and the step of dipping the pin.
2. A method according to claim 1, wherein the step of heating the pins includes heating the pins by radiant energy.
3. A method according to claim 1, wherein a group of pins are mounted on a bar, further including the step of heating the bar causing the group of pins to be heated by thermal conduction.
- 25
4. A method according to claim 3, wherein the step of heating the bar includes heating by thermal conduction from a plurality of thermally isolated deck segments.
5. A method according to claim 4, wherein the step of heating the bar includes heating a portion of the bar so as to maintain the temperature of the portion of the bar at a predetermined temperature.
- 30
6. A method according to claim 1, wherein the step of heating the pins includes heating the pins by thermal convection.
- 35
7. A method according to claim 1, wherein the step of heating the pins includes heating the pins within an

insulating enclosure.

8. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as 5 molds, comprising:

heating the pins;

greasing the pins;

dipping the pins into the solution to cause the 10 solution to gelatinize on the surface of the pins;

removing the pins from the solution;

drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and

removing the capsule bodies and capsule caps from the 15 pins;

wherein the step of heating the pins includes heating the pins by thermal convection after greasing the pins and before dipping the pins.

9. A method of manufacturing pharmaceutical capsules, 20 each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as molds, comprising:

heating the pins;

25 greasing the pins;

dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins;

removing the pins from the solution;

drying the gelatinized solution on the surface of the 30 pins to form capsule bodies and capsule caps; and

removing the capsule bodies and capsule caps from the pins;

wherein heating the pins includes heating the pins by radiant energy after greasing the pins and before the 35 dipping the pins.

10. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap,

- 40 -

from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as molds, a group of pins being mounted on a bar, comprising:

- heating the pins;
 - 5 greasing the pins;
 - dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins;
 - removing the pins from the solution;
 - 10 drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and
 - removing the capsule bodies and capsule caps from the pins;
- wherein heating the pins includes heating the group of pins via the bar after greasing the pins and before dipping the pins.

11. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as molds, comprising:

- heating the pins;
 - dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins;
 - removing the pins from the solution;
 - 25 drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and
 - removing the capsule bodies and capsule caps from the pins;
- wherein heating the pins includes heating the pins before dipping; and
- wherein drying the gelatinized solution includes heating the pins after dipping.

12. A method according to claim 11, wherein heating the pins after dipping includes heating the pins so that the capsule bodies and the capsule caps dry from the inside.

13. A method according to claim 12, wherein drying the gelatinized solution further includes performing

substantially all of the drying step within an enclosure having sides that are substantially closed.

14. A method according to claim 13, wherein drying the gelatinized solution further includes performing

5 substantially all of the drying step within an insulated enclosure.

15. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether 10 composition, using capsule body pins and capsule cap pins as molds, comprising:

heating the pins;

dipping the pins into the solution to cause the solution to gelatinize on the surface of the pins;

15 removing the pins from the solution;

drying the gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and

removing the capsule bodies and capsule caps from the pins;

20 wherein drying the gelatinized solution includes moving air in a direction opposed to the direction of movement of the pins within an enclosure that encloses the pins.

16. A method according to claim 15, wherein providing counterflow movement of air includes providing counterflow 25 movement of air over capsule body pins at one rate and counterflow movement of air over capsule cap pins at a different rate.

17. A method according to claim 15, further including the step of controlling the humidity of the air entering the 30 enclosure.

18. A method according to claim 17, further including the step of controlling the humidity of the air entering the enclosure within a range 0.006-0.012 lb water/lb air (0.6-1.2 percent).

35 19. A method according to claim 15, further including the step of controlling the temperature of the air entering the enclosure within a range 125°F-180°F (52°C-82°C).

- 42 -

20. A method according to claim 15, further including the step of heating the pins within the enclosure to achieve a predetermined air temperature profile within the enclosure.
- 5 21. A method according to claim 15, further including the step of controlling the flow of air within the enclosure to achieve a predetermined humidity profile within the enclosure.
- 10 22. A method according to claim 15, further including the step of agitating the air within the enclosure to minimize local air temperature differences and to speed local drying.
- 15 23. A method of manufacturing pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, from an aqueous solution of a thermogelling cellulose ether composition, using capsule body pins and capsule cap pins as molds, comprising:
- heating the pins;
- dipping the pins into the solution to cause the
- 20 solution to gelatinize on the surface of the pins;
- removing the pins from the solution;
- drying the gelatinized solution on the surface of the
- pins to form capsule bodies and capsule caps; and
- removing the capsule bodies and capsule caps from the
- 25 pins by gripping the capsule bodies and capsule caps between opposing gripping surfaces.
24. A method according to claim 1, further including cooling the solution to maintain the solution at a substantially constant predetermined temperature during
- 30 dipping.
25. An apparatus for the manufacture of pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, by dipping hot pins into an aqueous solution of a thermogelling cellulose ether composition, comprising:
- 35 a plurality of pinbars, each pinbar including a group of pins mounted on a bar;
- greaser means for greasing the pins;

- dipper means for dipping the pins into the solution;
spinner means for rotating and gyrating the pins after
they have been withdrawn from the solution;
dryer means for drying gelatinized solution on the
5 surface of the pins to form capsule bodies and capsule caps;
automatics means for removing the capsule parts from
the pins;
- transport means for moving the pinbars through the
greaser means, the dipper means, the spinner means, the
10 dryer means and the automatics means; and
heater means for heating the pins, including means for
heating the pins by thermal conduction via the bar.
26. An apparatus according to claim 25, wherein the
heater means includes means for heating pins selectively to
15 predetermined temperatures.
27. An apparatus according to claim 25, further
including a box having thermal insulating properties, the
box substantially enclosing the heater means.
28. An apparatus according to claim 27, further
20 including means for sensing and controlling the temperature
of a portion of the box.
29. An apparatus according to claim 25, further
including means for applying heat selectively to points
along the length of the bar.
- 25 30. An apparatus according to claim 25, wherein the
heater means includes means for heating the pins by thermal
convection.
31. An apparatus according to claim 25, wherein the
heater means includes a radiant heater.
- 30 32. An apparatus according to claim 25, wherein the
dipper means includes a dipper dish for capsule bodies and a
dipper dish for capsule caps; and wherein the dipper dish
for capsule bodies and the dipper dish for capsule caps are
35 spaced apart to accommodate the location of the heater means.
33. An apparatus for the manufacture of pharmaceutical
capsules, each capsule consisting of a capsule body and a

- 44 -

- capsule cap, by dipping hot pins into an aqueous solution of a thermogelling cellulose ether composition, comprising:
- a plurality of pinbars, each pinbar including a group of pins mounted on a bar;
- 5 dipper means for dipping the pins into the solution; spinner means for rotating and gyrating the pins after they have been withdrawn from the solution; dryer means for drying gelatinized solution on the surface of the pins to form capsule bodies and capsule caps;
- 10 automatics means for removing the capsule parts from the pins; transport means for moving the pinbars through the dipper means, the spinner means, the dryer means and the automatics means;
- 15 heater means for heating the pins prior to dipping; and an insulating enclosure substantially surrounding the spinner means; wherein the spinner means includes post-dip heater means for gelatinizing the solution on the pins.
- 20 34. An apparatus for the manufacture of pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, by dipping hot pins, as molds, into an aqueous solution of a thermogelling cellulose ether composition, comprising:
- 25 a plurality of pinbars, each pinbar including a group of pins mounted on a bar; dipper means for dipping the pins into the solution; spinner means for rotating and gyrating the pins after they have been withdrawn from the solution;
- 30 dryer means for drying gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; automatics means for removing the capsule parts from the pins; and transport means for moving the pins in a closed loop path through the dipper means, the spinner means, the dryer means and the automatics means;
- 35 wherein the dryer means includes an enclosure having

closed sides, the closed sides surrounding the pinbars within the dryer means.

35. An apparatus according to claim 34, wherein the dryer means further includes means for moving air through 5 the enclosure in a direction opposed to the direction of movement of the pins.

36. An apparatus according to claim 25, wherein the dryer means further includes means for supplying heat via the bar to the pins.

10 37. An apparatus for the manufacture of pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, by dipping hot pins, as molds, into an aqueous solution of a thermogelling cellulose ether composition, comprising:

15 a plurality of pinbars, each pinbar including a group of pins mounted on a bar;

dipper means for dipping the pins into the solution; spinner means for rotating and gyrating the pins after they have been withdrawn from the solution;

20 dryer means for drying gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; automatics means for removing the capsule parts from the pins; and

25 transport means for moving the pins in a closed loop path through means, the dipper means, the spinner means, the dryer means and the automatics means;

wherein the automatics means includes means for gripping a capsule part to remove the capsule part from a pin.

30 38. An apparatus according to claim 25, further including means for cooling the solution to maintain the solution at a substantially constant predetermined temperature during dipping.

35 39. An apparatus for the manufacture of pharmaceutical capsules, each capsule consisting of a capsule body and a capsule cap, by dipping hot pins into an aqueous solution of a thermogelling cellulose ether composition, comprising:

- a plurality of pinbars, each pinbar including a group of pins mounted on a bar;
- heater means for heating the pins;
- dipper means for dipping the pins into the solution;
- dryer means for drying gelatinized solution on the surface of the pins to form capsule bodies and capsule caps; and
- automatics means for removing the capsule parts from the pins;
- wherein the group of pins includes a pin for forming a capsule part having an open end, and the pin comprises:
- an elongated metal body;
- a domed head located at one end of the metal body; and
- a cylindrical sidewall surrounding the metal body and
- extending downwardly from the domed head, the sidewall having a diameter which varies along the length of the metal body such as to provide a taper with narrower dimension toward the head end of the body, a cut-point defining a cut-point diameter at a position along the length of the body at
- which the capsule part may be cut to form the open end;
- wherein the exterior shape of the pin is substantially the same shape as the inside of the cellulose capsule part and the cut-point diameter is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule part.
40. An apparatus according to claim 39, wherein the cut-point diameter of the pin for forming a capsule part is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule part by an amount in the range of approximately 0.7-2.0 percent.
41. An apparatus according to claim 40, wherein the cut-point diameter of the pin for forming a capsule part is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule part by approximately 1.3 percent.
42. An apparatus according to claim 39, wherein the cut-point diameter of the pin for forming a "0" size capsule

part is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule part by an amount in the range of approximately 0.002-0.006 inch (0.05-0.15mm).

5 43. An apparatus according to claim 42, wherein the cut-point diameter of the pin for forming a "0" size capsule part is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule part by approximately 0.004 inch (0.10 mm).

10 44. An apparatus according to claim 39, for forming a thick wall cellulose capsule cap, wherein the cut-point diameter of the pin for forming a capsule cap is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule cap by an amount in 15 the range of approximately 1.0-2.3 percent.

20 45. An apparatus according to claim 44, for forming a thick wall cellulose capsule cap, wherein the cut-point diameter of the pin for forming a capsule cap is smaller than the cut-point diameter of a pin used in the manufacture 25 of an equivalent size gelatin capsule cap by approximately 1.6 percent.

25 46. An apparatus according to claim 39, for forming a thick wall cellulose capsule cap, wherein the cut-point diameter of the pin for forming a "0" size capsule cap is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule cap by an amount in the range of approximately 0.003-0.007 inch (0.08-0.18 mm).

30 47. An apparatus according to claim 40, for forming a thick wall cellulose capsule cap, wherein the cut-point diameter of the pin for forming a "0" size capsule cap is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule cap by approximately 0.005 inch (0.13 mm).

35 48. An apparatus according to claim 39, for forming a thick wall cellulose capsule body, wherein the cut-point diameter of the pin for forming a capsule body is smaller

- 48 -

than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule body by an amount in the range of approximately 1.4-2.7 percent.

49. An apparatus according to claim 48, for forming a
5 thick wall cellulose capsule body, wherein the cut-point diameter of the pin for forming a capsule body is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule body by approximately 2.0 percent.

10 50. An apparatus according to claim 39, for forming a thick wall cellulose capsule body, wherein the cut-point diameter of the pin for forming a "0" size capsule body is smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule body by an
15 amount in the range of approximately 0.004-0.008 inch (0.10-0.20 mm).

51. An apparatus according to claim 50, for forming a thick wall cellulose capsule body, wherein the cut-point diameter of the pin for forming a "0" size capsule body is
20 smaller than the cut-point diameter of a pin used in the manufacture of an equivalent size gelatin capsule body by approximately 0.006 inch (0.15 mm).

52. A collection of capsules manufactured in accordance with the method of claim 1, each capsule in the
25 collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

53. A collection of capsules manufactured in
30 accordance with the method of claim 8, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

35 54. A collection of capsules manufactured in accordance with the method of claim 9, each capsule in the collection having sufficiently narrow dimensional tolerances

as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

5 55. A collection of capsules manufactured in accordance with the method of claim 10, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

10 56. A collection of capsules manufactured in accordance with the method of claim 11, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

15 57. A collection of capsules manufactured in accordance with the method of claim 12, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

20 58. A collection of capsules manufactured in accordance with the method of claim 13, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

25 59. A collection of capsules manufactured in accordance with the method of claim 15, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine.

30 60. A collection of capsules manufactured in accordance with the method of claim 23, each capsule in the collection having sufficiently narrow dimensional tolerances as to permit the filling of the capsules in a commercial

- 50 -

high-speed filling machine, the collection being large enough for a batch run on such filling machine.

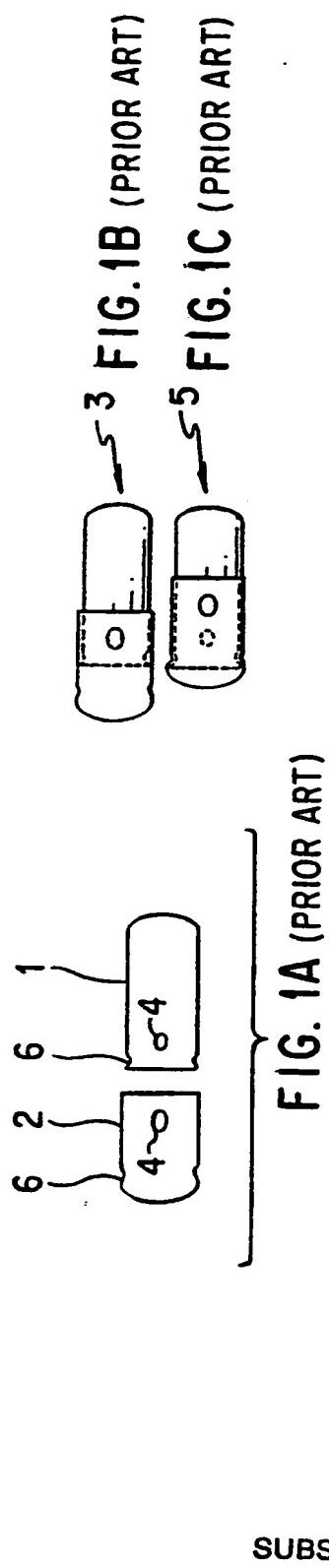
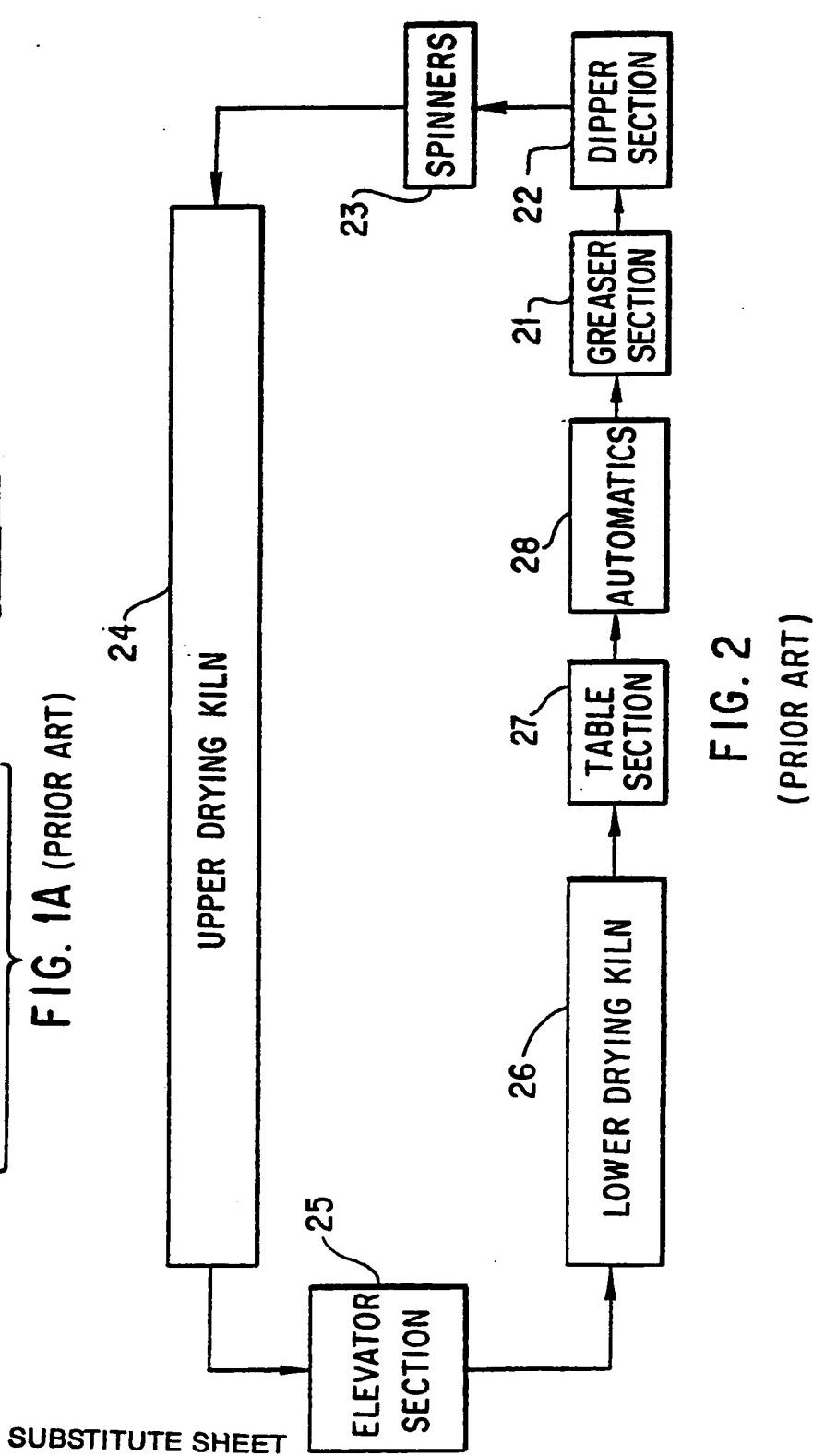
61. A collection of capsules for filling in a commercial high-speed filling machine, the collection being
5 large enough for a batch run on such filling machine, manufactured from an aqueous solution of a thermal gelling methyl cellulose ether composition, each capsule in the collection consisting of a capsule body and a capsule cap, the capsule body including a cylindrical wall whose
10 thickness is approximately 0.0046 inch (0.117 mm).

62. A collection of capsules for filling in a commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine, manufactured from an aqueous solution of a thermal gelling
15 methyl cellulose ether composition, each capsule in the collection consisting of a capsule body and a capsule cap, the capsule cap including a cylindrical wall whose thickness is approximately 0.0046 inch (0.117 mm).

63. A collection of capsules for filling in a
20 commercial high-speed filling machine, the collection being large enough for a batch run on such filling machine, manufactured from an aqueous solution of a thermal gelling methyl cellulose ether composition, each capsule in the collection consisting of a capsule body and a capsule cap,
25 the capsule body having a cylindrical wall including a stiffening ring.

64. A collection of capsules according to claim 61, wherein the cylindrical wall includes a stiffening ring.

1/15

**FIG. 1B (PRIOR ART)****FIG. 1C (PRIOR ART)**

2/15

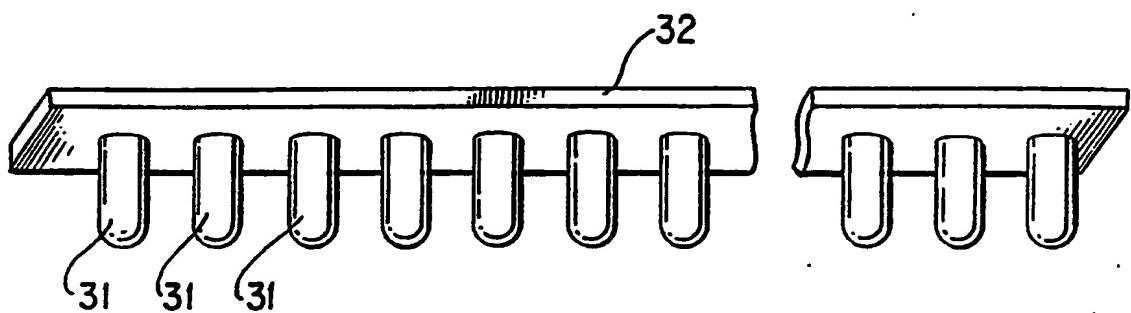


FIG. 3
(PRIOR ART)

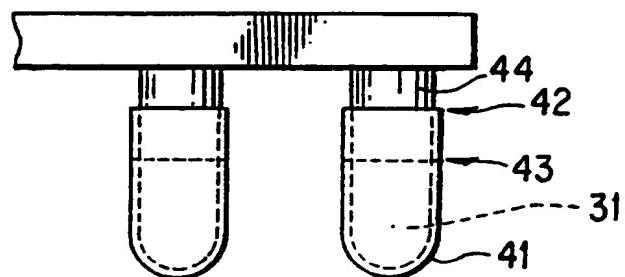


FIG. 4
(PRIOR ART)

SUBSTITUTE SHEET

3/15

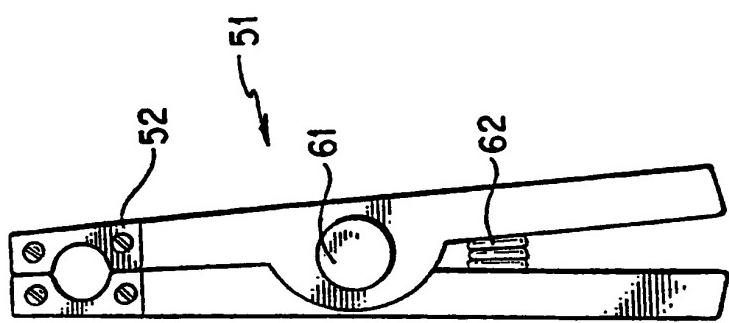


FIG. 6
(PRIOR ART)

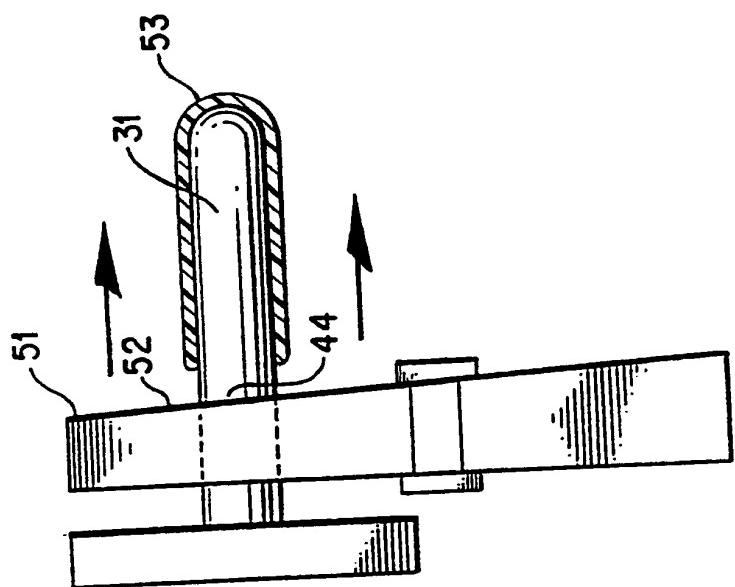


FIG. 5
(PRIOR ART)

SUBSTITUTE SHEET

4/15

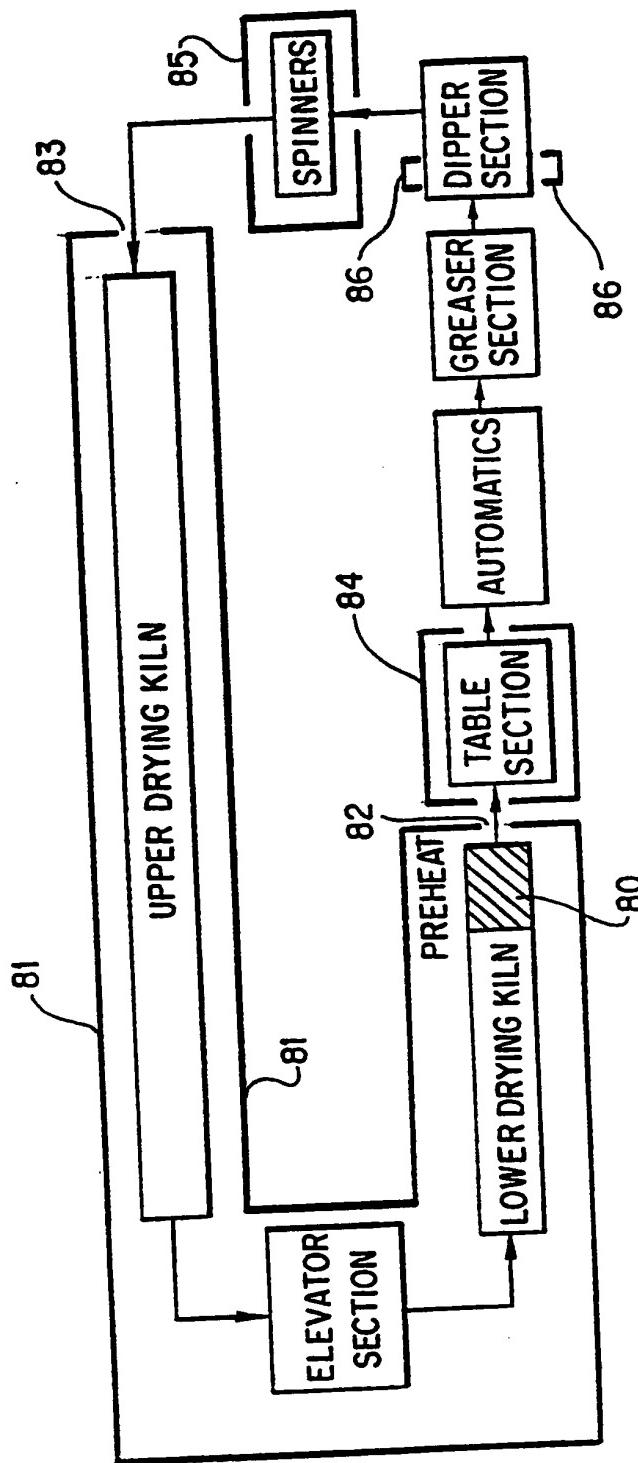
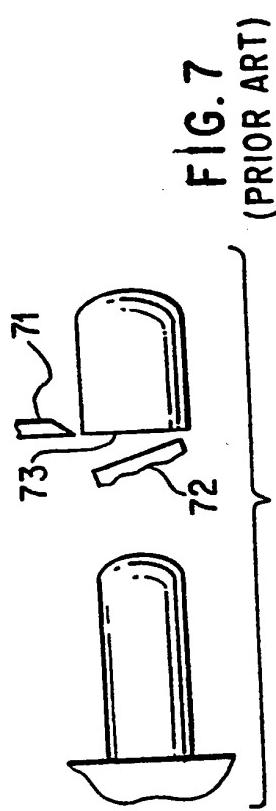
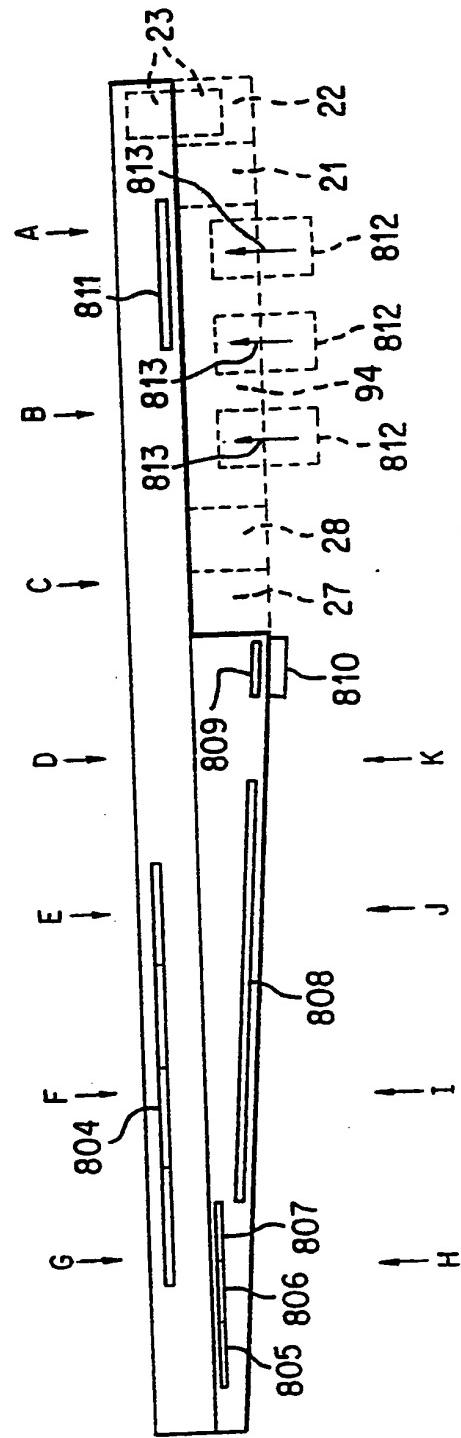
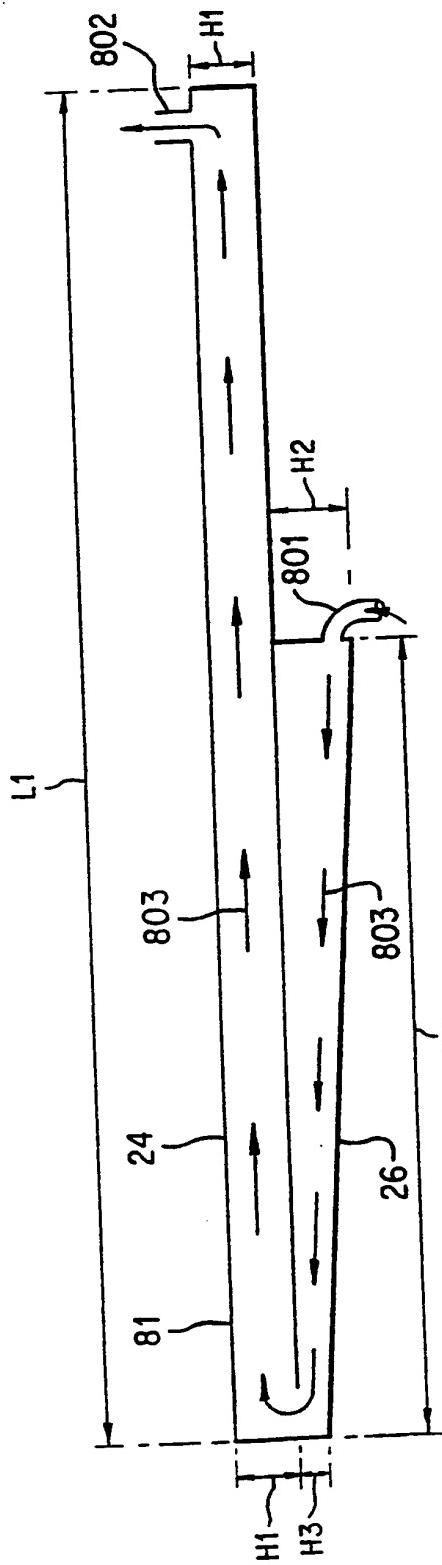


FIG. 8A

SUBSTITUTE SHEET

5/15



SUBSTITUTE SHEET

6/15

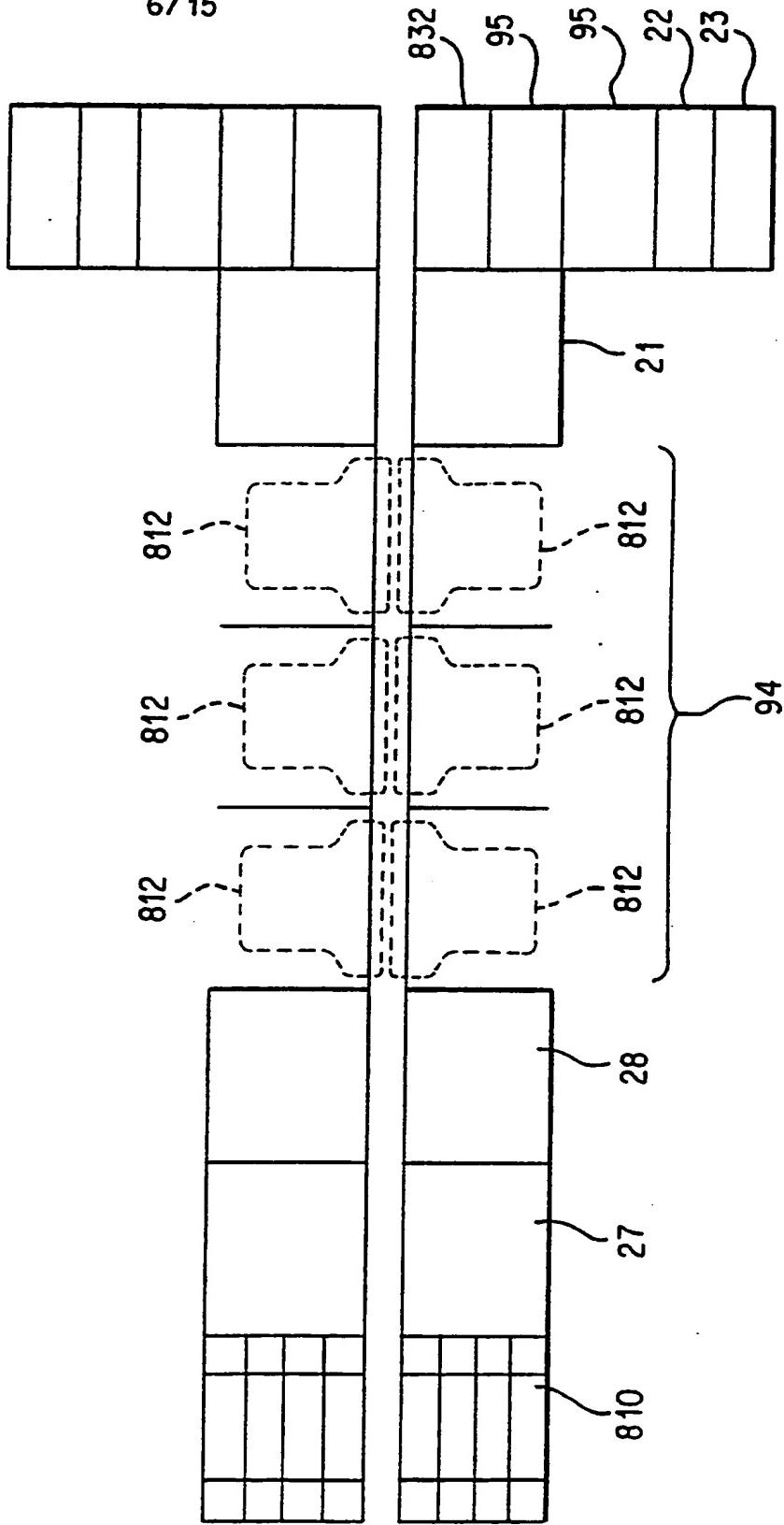


FIG. 8D

SUBSTITUTE SHEET

7/15

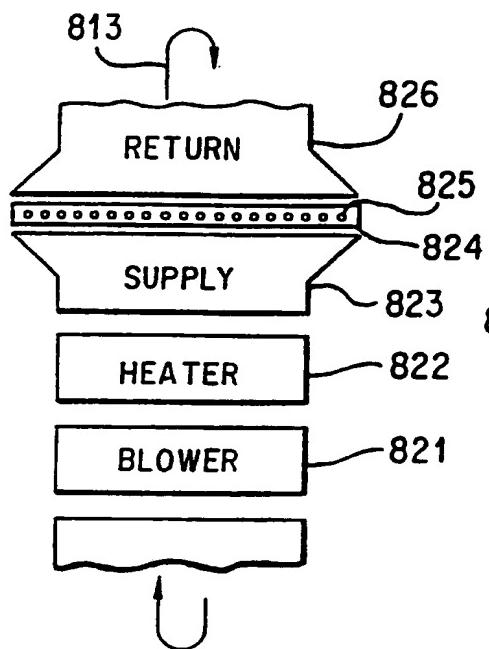


FIG. 8E

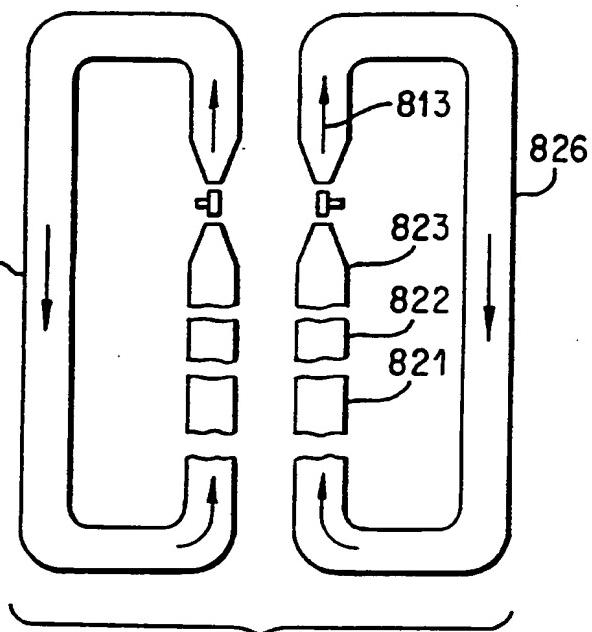


FIG. 8F

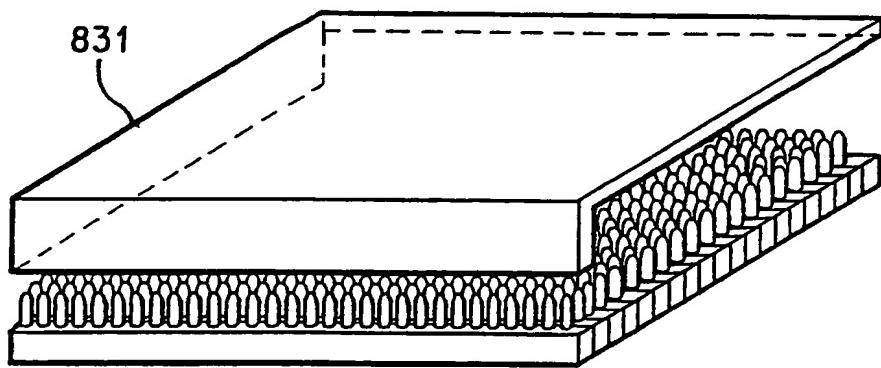


FIG. 8G

SUBSTITUTE SHEET

8/15

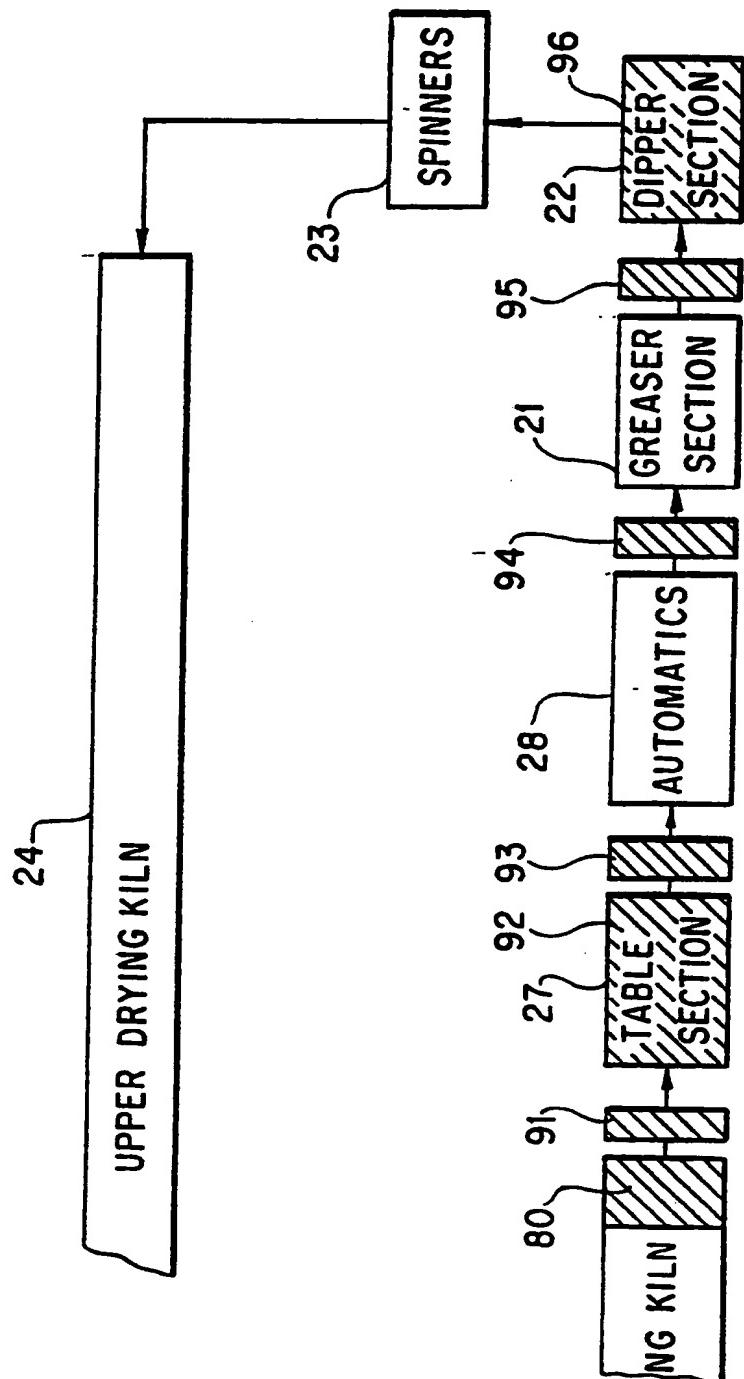


FIG. 9

SUBSTITUTE SHEET

9/15

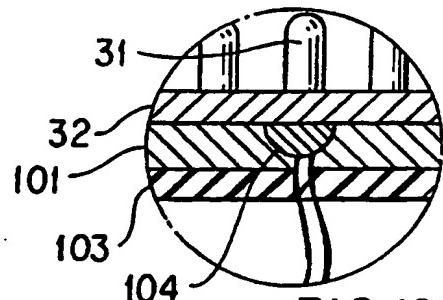


FIG. 10B

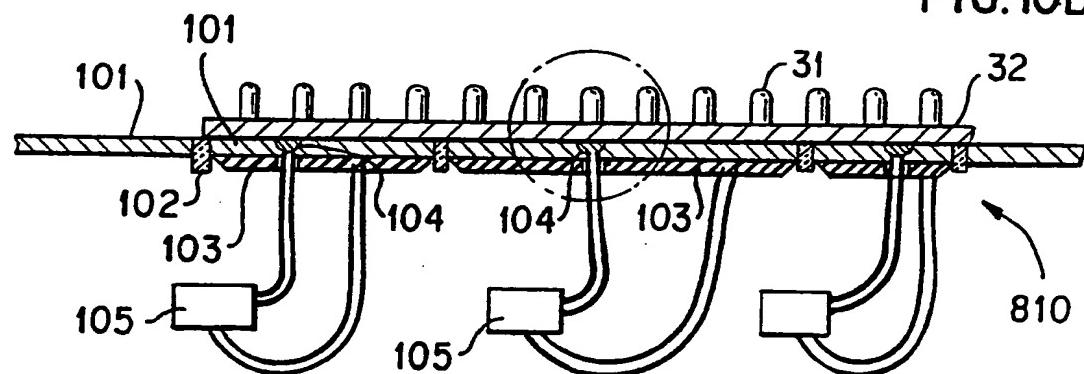


FIG. 10A

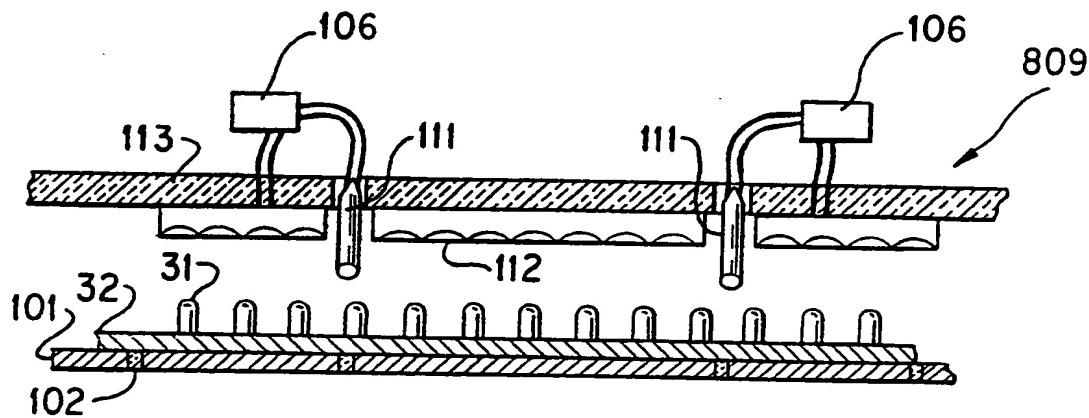


FIG. 11

SUBSTITUTE SHEET

10/15

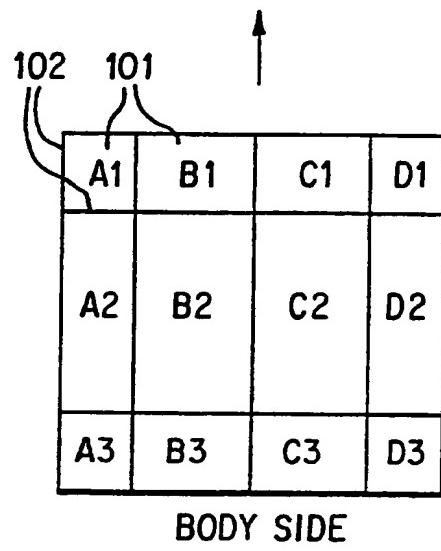
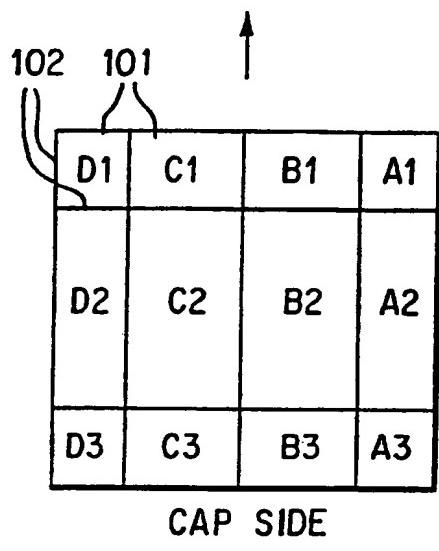


FIG. 10D

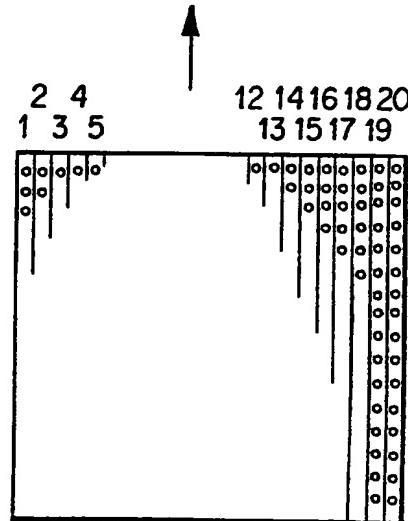
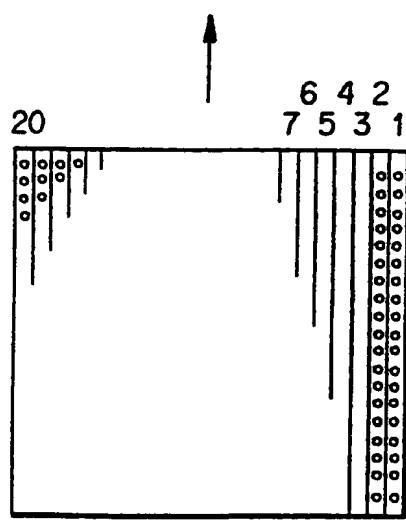


FIG. 10C

SUBSTITUTE SHEET

11/15

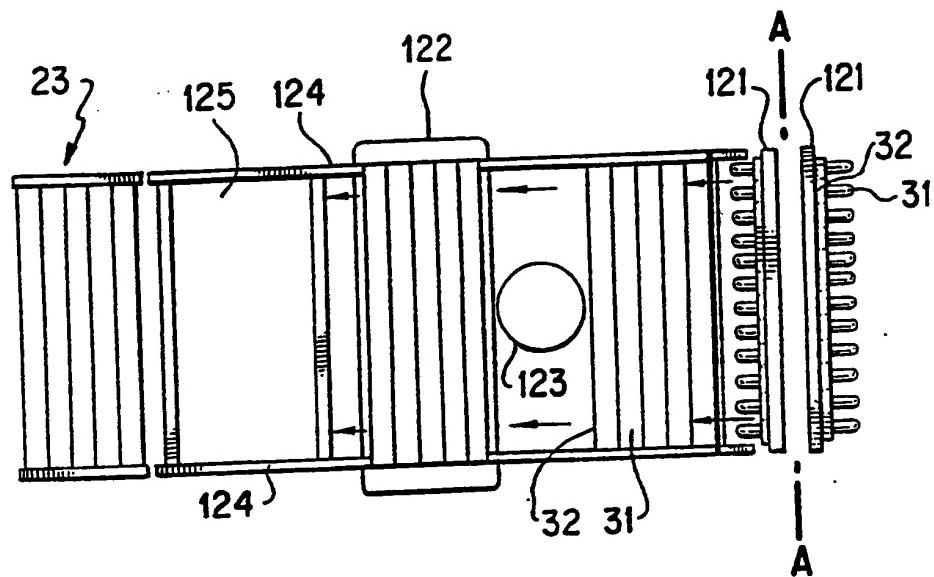


FIG. 12

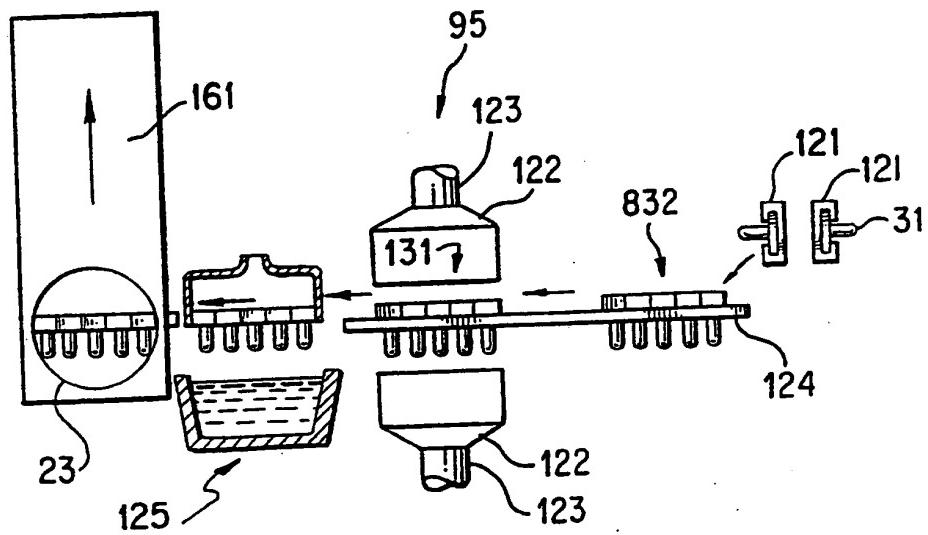


FIG. 13

SUBSTITUTE SHEET

12/15

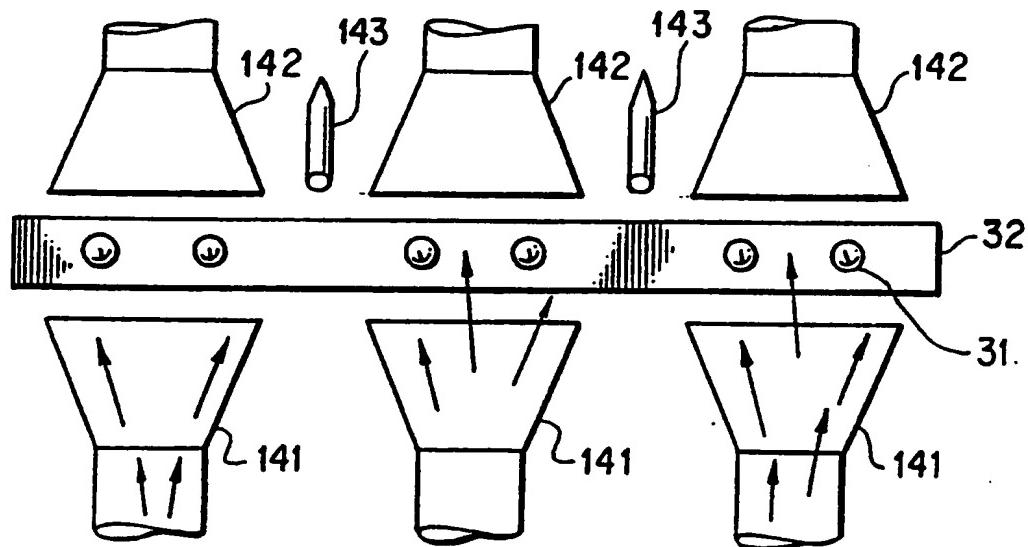


FIG. 14A

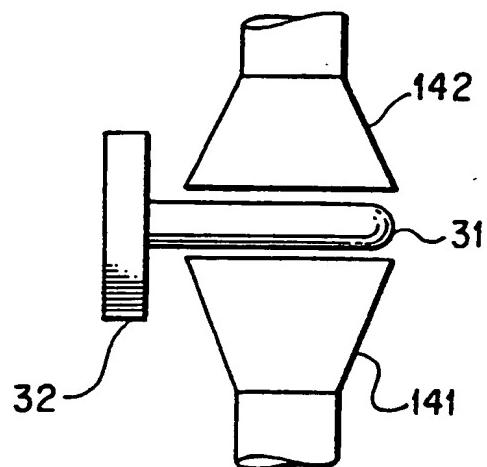


FIG. 14B

SUBSTITUTE SHEET

13/15

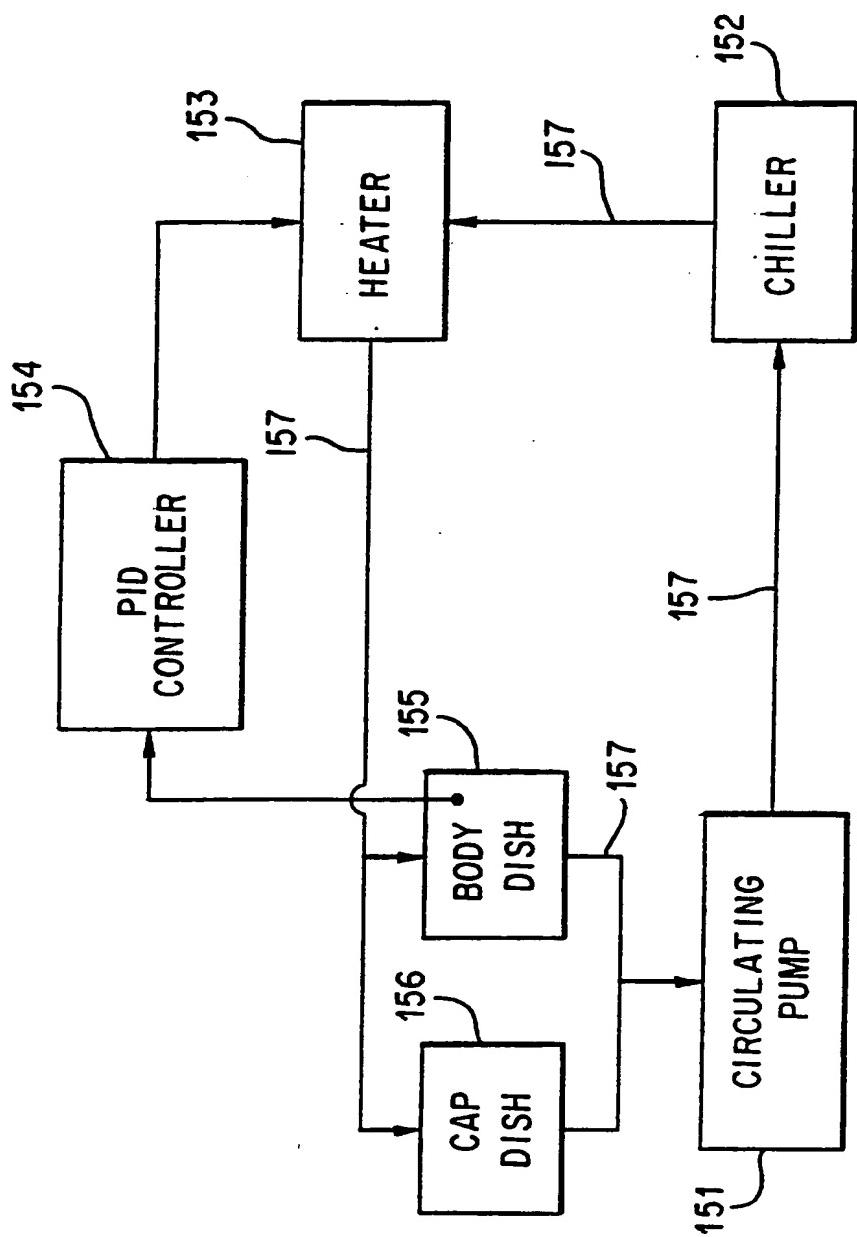


FIG. 15

SUBSTITUTE SHEET

14/15

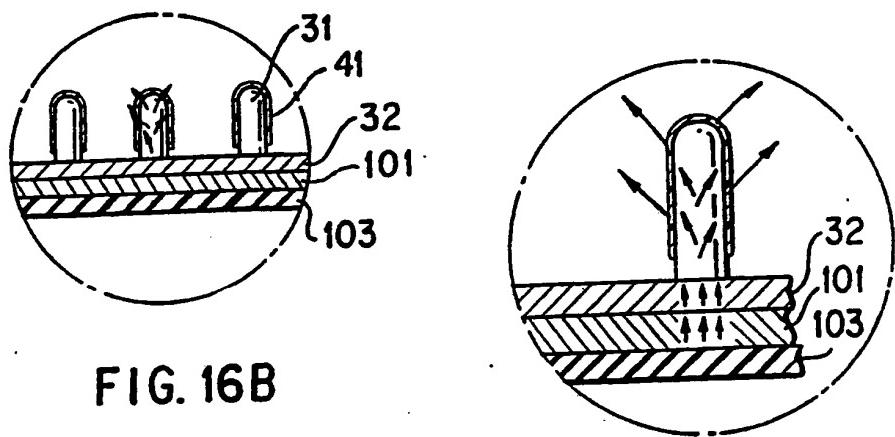


FIG. 16B

FIG. 16C

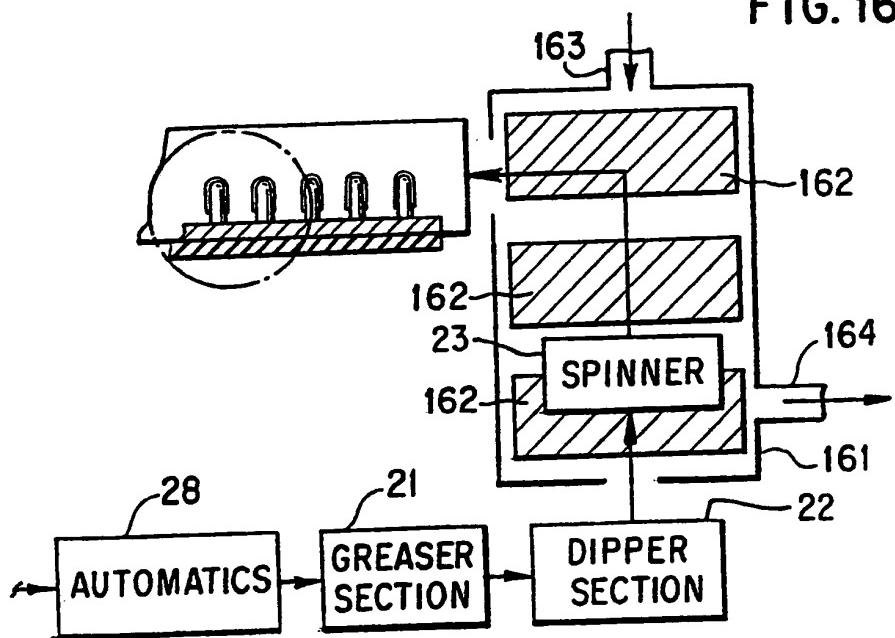


FIG. 16A

SUBSTITUTE SHEET

15/15

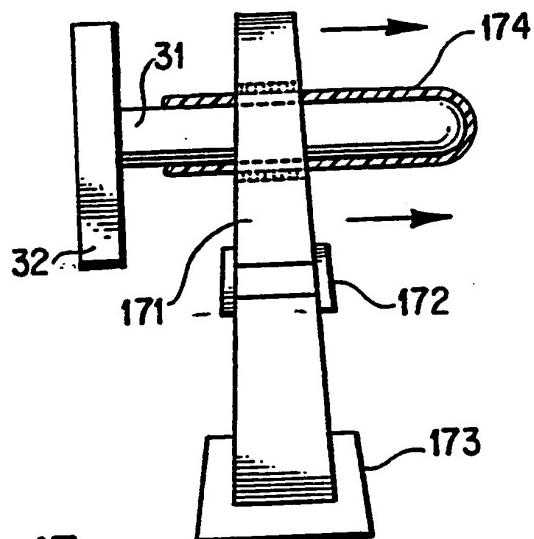


FIG. 17

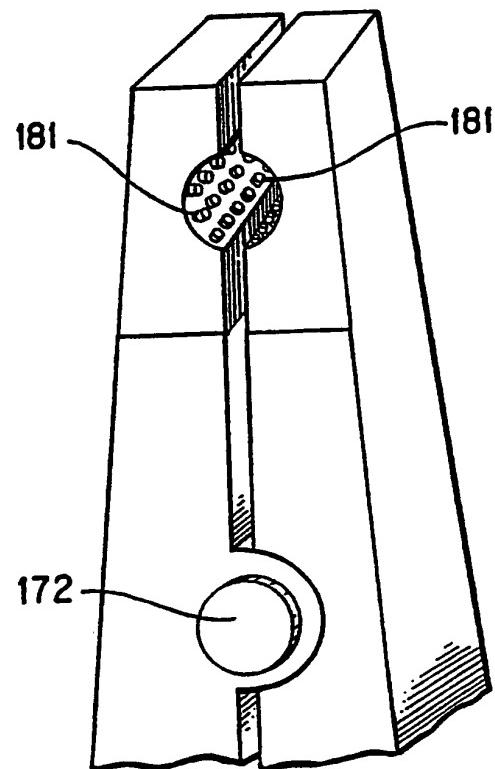


FIG. 18

SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International Application

PCT/US 92/04457

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC Int.Cl.5 A 61 J 3/07		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl.5	A 61 J	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	US,A,2671245 (KATH) 9 March 1954, see column 3, line 45 - column 4, line 38; column 6, lines 30-39; column 9, lines 54-61; figures (cited in the application) ---	1,2,9, 23,24, 37,38
X	US,A,1787777 (COLTON) 6 January 1931, see page 1, line 84 - page 3, line 11; figures (cited in the application) ---	1,23,24 ,37,38
X	US,A,4001211 (SARKAR) 4 January 1977, see column 5, lines 8-26 (cited in the application) ---	1,23,37 -/-
* Special categories of cited documents : ¹⁰ "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed		"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 03-08-1992	Date of Mailing of this International Search Report 03.11.92	
International Searching Authority EUROPEAN PATENT OFFICE	Signature of Authorized Officer GODOT T.G.L.	

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		Relevant to Claim No.
Category	Citation of Document, with indication, where appropriate, of the relevant passages	
A	US,A,3842242 (CHISHOLM) 15 October 1974, see claim 1; figures (cited in the application) -----	3-5,7, 10,25

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US92/04457

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

For further information see Form PCT/ISA/206 sent on 21.08.92.

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-10, 23-32; 36-38, 52-55 and 60

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.

US 9204457
SA 61031

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on 29/10/92.
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A- 2671245		None	
US-A- 1787777		None	
US-A- 4001211	04-01-77	CA-A- 1072445 DE-A- 2554164 GB-A- 1494868 JP-A- 51076417 NL-A- 7514012 SE-A- 7513519 BE-A- 836189	26-02-80 12-08-76 14-12-77 02-07-76 04-06-76 03-06-76 02-06-76
US-A- 3842242	15-10-74	None	